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THE JOURNAL

OF THE

American Medical Association

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VOLUME 127, No. 14
COPYRIGHT, 1945, BY AMERICAN MEDICAL ASSOCIATION
PUBLISHED WEEKLY

APRIL 7, 1945

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $8.00 a year. 25c a copy. Canadian $9.50. Foreign $12.00. Entered as second class matter June 25, 1835, at the Postoffice at Chicago, Ill., under Act of March 3, 1879. **Address all communications to American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois.**

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The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 127, No. 14 — CHICAGO, ILLINOIS — APRIL 7, 1945

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POTENTIAL DANGERS OF NONTOXIC NODULAR GOITER

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AND

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CHICAGO

Although the indications for surgical therapy are quite definite and generally agreed to in toxic diffuse goiter, the indications are less clear and urgent in nontoxic nodular goiter. Nevertheless it is well known that nontoxic nodular goiter may develop toxicity or be the site of carcinoma, although the incidence of these changes is not fully realized nor are the dangers appreciated. A study of patients in our clinic with carcinoma of the thyroid and nontoxic nodular goiter has convinced us that numerous complications (including particularly the two just mentioned) developing in this type of goiter may make surgical therapy quite urgent in this seemingly harmless lesion.

TYPES OF COMPLICATIONS RESULTING FROM NONTOXIC NODULAR GOITER

1. *Carcinoma.*—It is now agreed that carcinoma of the thyroid gland arises in adenomatous growths in the majority of instances; some workers make the rather dogmatic statement that 80 to 85 per cent of carcinomas arise in fetal adenomas, but we agree with Pemberton [1] that it is impossible to arrive at an accurate estimation of this relationship, largely because the tumor will overgrow the site of origin and thereby make it impossible to identify the original lesion where the carcinoma originated. In our series of 38 carcinomas (which represents a very small series encountered during the past seven years) we could with reasonable accuracy determine that the tumor arose in a fetal adenoma on 14 occasions (37 per cent). However, on many other occasions it is probable that the site of origin was likewise in a fetal adenoma, although the tumor had invaded the area so widely as to prevent identification of the original tissue. As indicated by Brenizer and McKnight,[2] cancer may arise also in colloid adenomas and diffuse adenomatous types, though perhaps less frequently. Lahey [3] has recently emphasized the importance of aberrant thyroid nodules in the development of carcinoma; in his series of 34 patients with aberrant thyroid tissue cancer was present in 35 per cent.

In our series the average duration of the thyroid mass in the patients with carcinoma was 7.1 years compared to 11.0 years in nontoxic nodular goiter and 13.9 years in toxic nodular goiter; in the former group there is commonly a history of sudden gradual growth during the past several months preceding the time when the patient sought medical care. However, this change in size is so commonly absent or ignored that the symptoms bringing the patient to the physician too commonly are voice change, difficulty in swallowing or breathing, or some other manifestation of invasion of carcinoma beyond its site of origin. Many authors writing on the subject make the bold statement that, once a carcinoma of the thyroid produces symptoms, it is beyond the possibility of a five year cure. Although this may not be entirely true, all would agree that the chances of a five or ten year cure are far better if the tumor is so early that it is not yet producing manifestations other than enlargement of the thyroid lobe.

Incidence: Carcinoma occurs so rarely in diffuse toxic goiter that inclusion of this type of lesion in the statistical study really confuses the issue. Ward [4] encountered only 1 carcinoma in 1,900 cases of toxic diffuse goiter; we encountered 1 in 435 cases of toxic diffuse goiter. Goetsch [5] found 8 carcinomas in toxic diffuse goiter but remarked that all arose in small adenomas.

The incidence of thyrotoxicosis (of all types) in our series of 38 cases of carcinoma encountered during the past seven years was 13.2 per cent. In a large series of carcinoma of the thyroid studied by Pemberton and Lovelace [6] thyrotoxicosis was present in 33.5 per cent of the group. However, the figure encountered in our series appears to be closer to the average, since many authors have encountered few or no instances of thyrotoxicosis. When thyrotoxicosis is present it is difficult to determine what tissue is responsible for it. However, after a study of 396 cases of carcinoma of the thyroid, with reference to thyrotoxicosis, Friedell [7] arrived at the conclusion that the carcinomatous area itself does not have the function of hyperthyroidism. We concur in this conclusion, believing that, when thyrotoxicosis is present, areas other than the carcinoma are responsible for the toxicity. This area might be either in the benign portion of the nodule or elsewhere in the parenchyma.

The incidence of carcinoma in nodular goiter varies somewhat throughout the country, suggesting that geographic sites play a role in development of malignant changes. In 2,324 patients with nodular goiter (toxic and nontoxic) Brenizer and McKnight [2] noted an inci-

From the Department of Surgery, University of Illinois College of Medicine, and the Illinois Research Hospital.

Read before the Section on Surgery, General and Abdominal, at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Pemberton, J.: Malignant Lesions of the Thyroid Gland, Surg., Gynec. & Obst. **69**: 417, 1939.
2. Brenizer, H. G., and McKnight, R. B.: True Adenomas and Their Relation to Cancer, Tr. Am. A. Study Goiter, 1940, p. 176.
3. Lahey, F. H.: Cancer of Thyroid, Am. J. Roentgenol. **46**: 469, 1941.
4. Ward, Robertson: Malignant Goiter, Surgery **16**: 783, 1945.
5. Goetsch, Emil: Incipient Carcinoma Occurring in Exophthalmic Goiter and Originating in Adenoma, Tr. Am. A. Study Goiter, 1940, p. 191.
6. Pemberton, J., and Lovelace, W. R., Jr.: Malignant Lesions of the Thyroid, S. Clin. North America **21**: 1037, 1941.
7. Friedell, M. T.: Hyperthyroidism and Adenocarcinoma of Thyroid Gland, Arch. Surg. **43**: 386 (Sept.) 1941.

dence of carcinoma of 4 per cent; in 3,539 cases of nodular goiter Ward [4] encountered carcinoma in 4.8 per cent of the group whereas we encountered carcinoma in 7.2 per cent of 523 patients with nodular goiter (table 1). These three reports illustrate the relative incidence in the widely distributed areas of the environs of North Carolina, California and Illinois, respectively.

TABLE 1.—*Incidence of Carcinoma in Various Types of Nodular Goiter (1936-1944)*

Of 523 nodular goiters (including toxic, nontoxic, benign and malignant)	7.2% were carcinoma
Of 330 nodular toxic goiters (including carcinoma)	1.2% were carcinoma
Of 247 multinodular toxic goiters	1.6% were carcinoma
Of 67 solitary nodular toxic goiters	0% were carcinoma
Of 192 nodular nontoxic goiters (including carcinoma)	17.1% were carcinoma
Of 100 multinodular nontoxic goiters	11.0% were carcinoma
Of 92 solitary nontoxic goiters	24.0% were carcinoma

There is also considerable variation in the age of the patients with carcinoma. Most authorities state that the age is similar to that of other types of carcinoma; for example, Pemberton and Lovelace [6] noted an average age of 48.1 in women and 52.8 years in men. On the other hand, the average age in our series, with a much higher incidence of carcinoma, was 42 years, indicating that as the incidence of cancer increases the tumor afflicts younger persons. It is, of course, well known that carcinoma of the thyroid, unlike carcinoma in most other organs, may appear in young people, including children. In 62 children 14 years of age or under with nodular goiter, Kennedy [8] encountered carcinoma in 12 cases, or 19.3 per cent of the group. All these carcinomas were in nontoxic nodular glands, indicating the serious aspects of nontoxic nodular goiter in childhood.

Goiter of all types is more common in women than in men, although the incidence in men is increased slightly in the carcinoma group over the incidence in nodular goiter. For example, in our series the incidence in women of toxic nodular goiter, nontoxic nodular goiter and carcinoma was 92.4, 89.3 and 84.0 per cent, respectively. Ward noted a ratio of 1 man to 7 women in benign nodular goiter but a ratio of 1 man to 3.5 women in carcinoma of the thyroid.

The incidence of carcinoma of the thyroid is much higher in nontoxic nodular goiter than in toxic nodular goiter, as illustrated by an incidence of 17.1 per cent

TABLE 2.—*Pathologic Types in Thirty-Eight Cases of Thyroid Carcinoma*

	Number	Per Cent
1. Adenoma malignum (with blood vessel and capsule invasion)	12	31
2. Papillary adenocarcinoma	11	29
3. Hürthle cell carcinoma	5	13
4. Diffuse adenocarcinoma	6	16
5. Small round cell diffuse carcinoma	2	5
6. Giant cell tumor	1	2.5
7. Type indeterminate (aspiration biopsy)	1	2.5

in 193 cases of the former group and only 1.2 per cent in 330 cases of the latter group (table 1). Another very important feature seldom mentioned in the literature, though referred to by Lahey,[3] is the fact that the solitary nodule is much more dangerous from the standpoint of malignant change than is the multinodular gland. Table 1 reveals that whereas only 11.0 per cent of cases of multinodular nontoxic glands were malignant, the astounding figure of 24.0 per cent of the nontoxic solitary nodules were the seat of carcinoma. In other words, every fourth patient in our series of solitary nontoxic nodular goiter (which constituted 70 per cent of the entire nontoxic nodular group) had a carcinoma, thus convincing one of the danger of conservative therapy particularly in this group.

Classification: Of the 38 cases of thyroid carcinoma herein reported, the distribution as to pathologic types is as listed in table 2. Details of classification of thyroid carcinoma may be found in a report by Warren.[9]

The relationship of fetal adenomas to the genesis of these malignant tumors cannot be accurately determined. As previously stated, it seems certain that at least 14 (37 per cent) of our cases had their origin in such a lesion. It is probable that several others did also, but the disease was so advanced in these cases that evidences of histogenesis were obliterated. In 2 of the cases of diffuse adenocarcinoma there were multiple benign fetal adenomas in the opposite thyroid lobe. At least 6 other cases arose from preexisting solitary, unilateral thyroid swellings which had been present from two to twenty-five years. These were more than likely fetal adenomas. Cases which we believe definitely arose in fetal adenomas varied histologically. The majority were of the type classified as "adenoma malignum," but others showed the histopathologic picture of papillary adenocarcinoma, diffuse adenocarcinoma and one of Hürthle cell carcinoma. Besides the 5 instances of Hürthle cell carcinoma reported here, there are in our files 4 cases of benign Hürthle cell adenoma.

TABLE 3.—*Five Year Survival Ratio in 231 Cases (Hare and Lahey)*

	Per Cent
Adenoma with blood vessel invasion	71
Papillary cystadenoma, malignant	62
Papillary adenocarcinoma	80
Alveolar adenocarcinoma	27
Small cell carcinoma	22
Giant cell carcinoma	17
Fibrosarcoma	33

The 12 cases of "adenoma malignum" constitute the equivocal pathology of thyroid cancer. The cases reported here were selected after careful study, in process of which a larger number of lesions were classified as hyperplastic fetal adenomas and discarded. The two criteria of invasion of the capsule and demonstrable tumor thrombi in veins (as emphasized by Graham [10]) were the bases of diagnosis in the doubtful cases. The most innocent looking lesion of the lot was in a patient whose symptoms were those of spinal cord compression. At laminectomy a thyroid tissue metastasis was found, and attention was directed to a small thyroid mass which turned out to be "adenoma malignum," eventually causing the patient's death.

Diagnosis: It is not our purpose in this paper to discuss the manifestations of carcinoma of the thyroid. Besides the presence of the tumor, which is usually firm, voice changes, difficulty in swallowing or breathing, "choking" attacks, cough and pain in the neck may be related to the local presence of the tumor itself. After metastasis has taken place numerous additional manifestations such as pain in the back or pelvis,

8. Kennedy, R. L.: Nodular Goiter Among Infants and Children, Tr. Am. A. Study Goiter, 1940, p. 322.

9. Warren, Shields: The Classification of Tumors of the Thyroid, Am. J. Roentgenol. **46**: 447, 1941.

10. Graham, Allen: Malignant Epithelial Tumors of the Thyroid with Special Reference to Invasion of Blood Vessels, Surg., Gynec. & Obst. **39**: 781, 1924.

hemoptysis, loss of weight or the development of masses elsewhere may appear.

Through coincidence alone a large percentage of asymptomatic thyroids will reveal carcinoma in its early stage. In our series the diagnosis was made only in the surgical pathology laboratory in 58 per cent of cases, in 21 per cent it was first made in the operating room and in another 21 per cent it was made clinically before therapy.

Treatment and Prognosis: It is agreed that operation combined with irradiation, preferably with radon seeds, is the treatment of choice in carcinoma of the thyroid. If any nodes are palpable elsewhere in the neck or if the tumor has invaded the capsule with penetration of adjacent tissue, a neck dissection is indicated. This operation should include excision of the strap muscles, the jugular vein and the sternomastoid muscle along with the lymphatics of the neck. Although the mortality rate in thyroidectomy for asymptomatic and clinically undiagnosed carcinoma will be no higher than in benign goiter, the rate will be considerably higher when a radical neck dissection is made necessary by invasion of adjacent tissue. Considering all types of operation for carcinoma of the thyroid, the mortality will vary from 1 to 4 per cent, depending largely on the frequency of radical neck dissections and the incidence of asymptomatic tumors.

Although irradiation is probably to be advised in the treatment of all thyroid carcinomas, yet it is really effective only in the papillary tumors, which fortunately are slightly more common than any other group, comprising 30 to 40 per cent of the entire group. In general, papillary carcinoma metastasizes more slowly than most other types, five year cures being obtained by many authors in 70 to 80 per cent of this type. The five year survival rate in 231 cases as reported recently by Hare [11] and Lahey [3] is so significant that it is reproduced in table 3.

The important role of early diagnosis and treatment on ultimate results is borne out by the observations of Ward,[4] who noted that five year cures were obtained in only 20 per cent of cases diagnosed before operation, in 40 per cent if the tumor was diagnosed at operation and in 80 per cent when the diagnosis was first made in the Surgical Pathology laboratory.

2. *Development of Toxicity.*—It is well known that thyrotoxicosis may be superimposed on nontoxic nodular goiter. In our study, which included 326 cases of benign toxic nodular goiter, the average duration of the nodule before toxicity developed was 9.37 years; the average duration of symptoms was 3.53 years. Symptoms of toxicity develop so insidiously in toxic nodular goiter that the patients usually have symptoms quite some time before they come to the physician. No doubt toxicity was present in many of these patients long before they actually detected any of its manifestations. Development of toxicity in nodular goiter in children is practically unknown, in contrast to the high incidence of development of carcinoma in nodular goiter in children. It is very difficult to estimate just what proportion of patients with nontoxic nodular goiter would develop toxicity. Naturally, the percentage would change with the duration of the mass. The fact that 11 per cent of our patients with nontoxic nodular goiter were past 50 and that 29 per cent of our patients with toxic nodular goiter were past 50 is definitely suggestive that as the patient becomes older there may be a definite increase in the trend toward development of toxicity. Wetherell [12] has estimated that 50 per cent of patients with nontoxic nodular goiter would ultimately become toxic if left untreated. The authors agree that this figure would appear reasonable. The fact that we encountered almost twice as many toxic nodular goiters as nontoxic nodular goiters in a given period cannot be considered as an indication of the frequency of toxicity, since there will be less tendency for patients with nontoxic nodular goiters to seek medical aid.

There is considerable controversy as to the frequency of development of thyrotoxicosis in nodular goiter under iodine medication. In reality there should not be any indication for giving iodine to a patient with nontoxic nodular goiter, since goiter of this type does not regress

Large nontoxic nodular goiter in a Negro woman aged 32. Goiter of this type is much less likely to produce serious compression symptoms than would a much smaller carcinoma. However, this patient had mild interference with breathing, particularly when lying down.

under iodine as usually occurs in nontoxic diffuse goiter. However, many patients themselves will take iodine, having heard that iodine is good for goiter; on other occasions physicians prescribe it under the impression that the goiter is of the diffuse nontoxic type, which does respond to iodine. In general, it may be said that development of toxicity secondary to iodine is quite uncommon. However, one of us (W. H. C.) observed its occurrence in a woman aged 23 who developed severe toxicity from a nontoxic nodular goiter under iodine medication, which completely disappeared with cessation of iodine therapy.

3. *Local Effects of Nodular Goiter.*—Although the local effects produced by nontoxic nodular goiter are

11. Hare, H. F.: Radiation Treatment of Cancer of the Thyroid, Am. J. Roentgenol. **46**: 451, 1941.

12. Wetherell, F. S.: Inherent Dangers in Nodular Goiter, J. Internat. Coll. Surgeons **4**: 248, 1941.

much less common than those encountered in carcinoma of the thyroid, yet a significant percentage of patients with nontoxic nodular goiter coming for treatment will complain of pressure manifestations. In our experience about 20 per cent complain of pressure symptoms in addition to the mere presence of the mass. This incidence may be rather high, since our patients are charity patients and therefore come to the physician relatively late. The most common and earliest complaint is a choking sensation which frequently awakens the patient from his sleep. During the relaxation of sleep, certain muscles which tend to maintain an adequate airway become relaxed and allow the mass to compress the trachea or larynx. A few of the patients actually complain of difficulty in breathing and may actually have a stridor. Less commonly, difficulty in swallowing is a complaint. Voice changes are not infrequent and may be due either to pressure on the larynx or to pressure on the recurrent laryngeal nerve with a consequent paresis or paralysis. Actual paralysis of the nerve is relatively uncommon in nontoxic nodular goiter but does occur. Pain is rarely complained of except that it may be produced when the neck is turned in certain directions. In many patients the cosmetic appearance alone is sufficient to bring them to the surgeon for removal of the mass.

4. *Systemic Manifestations.*—Ordinarily one thinks of nontoxic nodular goiter as producing few or no systemic manifestations. Yet the gradation between nontoxic and toxic nodular goiter is so narrow that it is extremely difficult to set up criteria which can be used to identify borderline cases specifically as toxic or nontoxic. In the classification herein discussed we have adopted the same criteria as have others, namely that the nontoxic nodular group has a basal metabolic rate less than plus 10 or 15 and has no symptoms such as significant nervousness, cardiac decompensation or sweating. Nevertheless in about 20 per cent of our nontoxic nodular group one or more mild symptoms such as slight nervousness, tachycardia, weakness, dyspnea and increase in sweating were encountered. These symptoms develop so insidiously and may be so mild that they are scarcely appreciated by the patient until after operation, when pronounced improvement is noted. Most of these patients have large degenerating goiters and are in the latter decades of life. Many surgeons, including Lahey,[13] Wetherell [12] and Hicken,[14] have expressed the same or similar thoughts. The development of heart disease, including decompensation with or without fibrillation, is quite common in toxic nodular goiter and in that disease represents the most serious complication or sequela. Heart disease supposedly should not exist in nontoxic nodular goiter, although Hertzler [15] has been a strong advocate of the removal of this type of growth for its beneficial effect on the heart itself. The question immediately arises as to whether or not these patients with supposedly nontoxic nodular goiter who are relieved of symptoms by removal of the growth might not actually be toxic. In going over the patients in our series we were amazed at the large number of cases which presented difficulty in diagnosis from the standpoint of toxicity. As stated, about 20 per cent of our group of patients with nontoxic nodular goiter had a few symptoms, such as nervousness, slight tachycardia and sweating, which were suggestive of hyperthyroidism but by no means conclusive. In this group the basal metabolic rate is of little diagnostic value. We are convinced, however, that the great proportion of these should be classified as toxic goiters, realizing that almost every disease manifests itself in different stages, including very mild degrees as well as severe degrees of intensity.

TABLE 4.—*Characteristics of Various Types of Nodular Goiter, Including Carcinoma (1936-1944)*

Type of Lesion	Total No.	Average Age	Sex, per Cent Females	Race, per Cent Colored	Duration Mass, Yrs.	Number Solitary
Toxic nodular goiter (benign)	326	43.3	92.4	7.7	13.9	67 (21.0%)
Nontoxic nodular goiter (benign)	159	41.1	89.3	11.3	10.0	70 (44.0%)
Carcinoma of thyroid	38	42.0	84.0	16.0	7.1	22 (57.8%)
Total.....	523					

TABLE 5.—*Carcinoma of the Thyroid (Total Cases 38)*

33, or 86.8%, were in nontoxic nodular goiters (22 in solitary nodular goiters and 11 in multinodular goiters)
4, or 10.5%, were in toxic nodular goiters (all were in multinodular goiters)
1, or 2.6%, was in toxic diffuse goiter

SUMMARY

In view of the wide variation of opinion as to the indications for operation in nontoxic nodular goiter, we have made a clinical study of "goiter" patients admitted to Illinois Research Hospital, hoping to obtain information which might determine how urgently we should advise surgical therapy in this lesion. The development of four major types of complications, including (1) carcinoma, (2) thyrotoxicosis, (3) local (pressure) symptoms and (4) systemic manifestations, is encountered. Of this group carcinoma is unquestionably the most significant. In the entire group of 523 patients with nodular goiter (including benign, malignant, toxic and nontoxic) encountered in our hospital during the past seven and one-half years there was an incidence of carcinoma in 7.2 per cent of the cases. In 330 toxic nodular glands there was an incidence of only 1.2 per cent of carcinoma; in this toxic group carcinoma was not encountered in a single patient with a solitary nodule. In 192 patients with nodular nontoxic goiter there was an incidence of carcinoma in 17.1 per cent of the cases. The most astounding feature is that in the group of patients with nontoxic nodules carcinoma was found in 24.0 per cent. In patients with multinodular nontoxic goiters the incidence was 11.0 per cent. Since all of our patients are charity patients, the incidence of carcinoma would no doubt be higher than in a similar study conducted in a private hospital, because charity patients tend to neglect their diseases much longer than private patients. In the patients with solitary carcinoma the average duration of the mass before admission was 7.1 years. The average age was 42.0 years, almost identical to the average age of the patients with nontoxic nodular and toxic nodular goiter, and distinctly lower than the average age in cancer of most other organs; the frequent occurrence of carcinoma of the thyroid in young people, including children, is well known.

Although most authorities believe that carcinoma of the thyroid arises from adenomas (primarily the fetal type) in 60 to 90 per cent of cases, it is impossible to

13. Lahey, F. H.: Surgery in Hyperthyroidism, Tr. Am. A. Study Goiter, 1938, p. 297.
14. Hicken, N. F.: Should Quiescent Adenomatous Goiters Be Removed? Rocky Mountain M. J. **37**: 94, 1940.
15. Hertzler, A. E.: Diseases of the Thyroid, New York, Paul B. Hoeber, Inc., 1941.

arrive at a correct decision as to frequency, since the tumor so often has overgrown the original site. In 37 per cent of our cases of carcinoma we were able to discern with accuracy that the tumor arose in a fetal adenoma. Without question it arose from a fetal adenoma in many other cases (perhaps twice as many) although proof cannot be obtained.

Goiter of all types is more frequent in women than in men; about 90 per cent of patients with nodular goiter (nontoxic and toxic) are women. In carcinoma the feminine incidence is slightly lower, women constituting 84 per cent of the group.

Fortunately, if the policy of removing a great portion of nontoxic nodular goiters is adopted, many instances of carcinoma will be found when no clinical manifestations of the tumor existed. In our series 58 per cent were diagnosed only after examination in the Surgical Pathology laboratory; the diagnosis was made on the operating table in 21 per cent of cases and before operation in 21 per cent.

The results of treatment which consists primarily of excision and radiation (preferably radon seeds) in patients with carcinoma of the thyroid are remarkably good. Of the major types of carcinoma treated as just described, a five year cure can be expected in over 50 per cent of cases. Needless to say, the five year cure figure will be much higher in the group showing no clinical manifestations. Ward's figures of 20 per cent five year cure in patients diagnosed before operation and of 80 per cent in patients diagnosed only after examination of the specimen in the Surgical Pathology laboratory proves emphatically the advantages of early or prophylactic therapy.

There is no way of arriving at a correct figure as to the likelihood of development of toxicity in a nontoxic nodular goiter. However, we would estimate that, if left untreated, about 50 per cent of nontoxic nodular goiters would ultimately develop some degree of toxicity. This tendency toward development of toxicity is entirely absent in childhood and appears to increase with increase in age, particularly in the latter decades of life.

After completion of this study we have reached the conclusion that, in general, solitary nontoxic nodular goiters in young people should be removed surgically, because of the danger of development of carcinoma or thyrotoxicosis, particularly the former.

ABSTRACT OF DISCUSSION

DR. FRANK H. LAHEY, Boston: The mortality of removal, particularly in the type of adenoma that is likely to become malignant, ought to be zero because it is a discrete adenoma and easily removed. These patients are in the hospital not over a week, so why trade the hazards of malignancy in a thyroid adenoma of this type when there is no risk and the hospital stay is so short? My associates and I have had a large experience with thyroid adenomas that have become malignant. The size of these adenomas is of no importance. We have seen an adenocarcinoma in a discrete adenoma the size of my little fingernail. Age is of no importance. We have had a boy of 9 years die of carcinoma of the thyroid, and several patients were 12, 13 and 14 years of age. More mistakes are made as relates to malignancy in the diagnosis of aberrant thyroid glands than in almost any single factor in thyroid states. Adenomas should not be ruptured in removing them because it is not known at the time of removal whether or not they are malignant. A particular characteristic of malignancy of the thyroid is to invade veins, and Allen Graham has emphasized that in any radical removal all adjacent veins must be removed. If carcinoma of the thyroid has eroded through the capsule with parenchymatous involvement, then not only is there involvement of lymph nodes but often extension into the neighboring veins. If we find a carcinoma of the thyroid involving one lobe we take out the sternomastoid on that side and the internal jugular from above to below the gland and all of the lymph nodes and thyroid on that side. The ideal treatment of carcinoma of the thyroid is the combination of radical surgery and high voltage x-rays. If these dissections are extensive, we carry out tracheotomy at the time of operation because a well done tracheotomy situated low on the trachea will not cause trouble. If tracheotomy is not done and intense radiation is given, there will be severe reactions and tracheotomy will have to be performed as an emergency. When a prophylactic tracheotomy is done the patient is comfortable, and one can do as much as one chooses in the way of postoperative irradiation. Patients with toxic adenomas are in the group in which the greatest number of unexpected fatalities occur, and so in these cases the greatest surgical judgment must be employed. Thiouracil will lower the metabolic rate in patients with toxic adenomas as it will in patients with primary hyperthyroidism. By the use of thiouracil we do not change the histologic picture of hyperthyroidism in the least; the drop in the metabolic rate which is obtained by its use is an extra thyroid effect and probably but a temporary one and not a method of curing patients of hyperthyroidism but a method of preparing them for safer operation. We have now employed thiouracil for patients with toxic thyroids for over a year and we know the great difficulty of operating on these patients since thiouracil does not involute the thyroid gland. Although it lowers the metabolic rate it makes the operation of subtotal thyroidectomy as technically difficult as it was when we used to operate on patients before we had Lugol's solution. The bleeding is almost uncontrollable and the gland is so friable in these thiouracil patients that the operation is definitely prolonged. Dr. Bartels, in our clinic, has now for some time employed a plan for these cases which overcomes these difficulties, first dropping the metabolic rate with thiouracil and then giving Lugol's solution for about two weeks. The Lugol's solution will so devascularize and involute the gland that these disadvantages are overcome. If thiouracil is given indiscriminately it possesses the danger of producing agranulocytosis, kidney damage, allergic reactions and skin changes, but it is valuable and will prove to be a useful addition to our armamentarium.

DR. GEORGE M. CURTIS, Columbus, Ohio: There is a complication which should receive our attention: that of hemorrhage into the nodular goitrous gland. Along with nodule formation occur vascular degenerative changes. In regions where nodular goiter is common these may occur early in life. Resultant hemorrhages of a mild degree are often seen during the dissection of the goitrous mass removed by thyroidectomy. In their more severe form these hemorrhages are the principal cause of cyst formation. The content of these larger cysts, and particularly of those developing within the mediastinum, is high in iron and low in iodine, indicating the hemorrhagic origin. The mechanical effects of these larger cysts, especially by pressure on the trachea, is obvious. Atherosclerotic changes may often be demonstrated in the arteries of older nodular goiters. Rupture of these damaged thyroid vessels with resultant acute severe hemorrhage is uncommon but well recognized. About 50 instances have been reported in which death resulted from the resultant pressure on the trachea. The recognition of incipient toxicity and of the lesser degrees of hyperthyroidism has long presented a problem. Determinations of the basal metabolic rate are not wholly sufficient, since hypermetabolism does not necessarily mean hyperthyroidism. Definite progress has been made in developing determinations of the protein bound iodine of the blood. These, more nearly than anything else I know, give an index of the degree of thyroid activity. This represents an approach to the determination of the circulating thyroid hormone. Although this method is well developed, it is difficult to apply. Nodular goiter now appears largely as a preventable disease. Of the various goitrogenic agents now known, the principal one is an insufficiency of available iodine. In geographic regions where goiter is common the iodine intake is low. Moreover, the excretion of iodine is considerably less than that of individuals in regions where goiter is infrequent. Since thyroxin is two thirds iodine, the thyroid gland must have

an adequate iodine supply properly to make sufficient thyroid hormone. We should consider iodine deficiency as related to the incidence of nodular goiter. Geographic studies, the determination of the usual rate of thyroxin formation and decay and human iodine balance studies have given a fairly clear idea of human iodine requirements. Allowing for some reserve for extra demands, this is daily about 3 micrograms of iodine per kilogram of body weight. More is required during pregnancy, since the developing fetus should also have a sufficient supply. This need is more than adequately supplied by the use of the current iodized salt. Since nodular goiter appears to be a genetic disease, it is even more important to such families or in those regions where the endemism is severe and the consequent incidence of nodular goiter with its complications is high.

DR. BRIEN T. KING, Seattle: I have operated with 100 per cent cure on 35 persons with carcinoma of the thyroid, all of whom are still living and well, and I do not treat them with any radiation thereafter. I do not think I have cured a single patient with diffuse carcinoma of the thyroid, though a number of them are still living after years. I suspect that those that are living sooner or later, if they don't die of an intercurrent condition, will have a recurrence of carcinoma of the thyroid. The time of recurrence depends on the degree of malignancy. I would further subdivide the encapsulated carcinomas in children. I make an arbitrary age of 12 years instead of 14, because adolescence certainly begins to play an earlier and effective role on the changes that take place in the dormant adenomas that sometimes exist in children prior to that age, and of the single discrete adenomas of the thyroid that have occurred in certain children in my experience under 12 years of age a large percentage have been malignant, but only one of them has been a diffuse malignancy. By that I mean that the carcinoma extended through the capsule and invaded the rest of the glands, and among the 35 who are cured some were children. Two of them were children under 10 years of age and 3 or 4 more under 12 years of age. The diagnosis of nontoxic adenoma is much more often made erroneously than the diagnosis of simple and nontoxic adenoma, and the only way one can really make a diagnosis of a nontoxic nodular goiter is by the clinical history, particularly if one finds that that patient is 45 or 50 or 55 or 60 years of age. If one finds that in some time during the last ten or fifteen or twenty years there has existed a goiter and there is a history of toxic goiter one had better get it out. I wish to call attention to an increased heart consciousness in the presence of adenomatous goiter and to the irregularity of the heart. A majority of all the auricular fibrillations that occur in the state of Washington are due to toxic goiter. Extrasystoles are often the prodrome of auricular fibrillation. If one finds a patient with an adenomatous goiter or nodular goiter and an irregular heart action, remove it. My experience has been that in 99 per cent of them that irregularity of the heart will disappear in from ten to ninety days.

DR. DANELY P. SLAUGHTER, Chicago: There are few epithelial organs in the body which produce such a variety of tumors as does the thyroid. There are many different classifications of thyroid tumors, but the most equivocal pathologic condition is that of the so-called encapsulated adenomas. In the doubtful cases our criteria for diagnosis of these malignant adenomas, or the encapsulated lesions which we have considered as cancer, are those of invasion of the capsule and demonstrable tumor thrombi in the veins. The definitive treatment of thyroid cancer is surgical. The results of irradiation alone have been very poor. With external x-radiation it is almost impossible to sterilize thyroid cancer. Unquestionably a small residual or irremovable area of carcinoma can be completely obliterated by radon seeds. Enough seeds can be put in any area of tissue in the body to destroy it completely. It is the residual tissue which one can't see that so often defeats one. I don't believe in postoperative irradiation after removal of a so-called encapsulated carcinoma. If a cancerocidal dose is delivered into the neck, considerable damage to the tissue results without definite evidence that any cancer has been treated. Since these solitary nontoxic adenomas are the dangerous type from the standpoint of cancer, it would be better that we deliberately do a total hemithyroidectomy rather than simply "shell out the tumor." When thyroid carcinoma has been diagnosed clinically we would recommend a formally planned total thyroidectomy and radical neck dissection on the side involved. The radical neck dissection should include removal of the internal jugular vein, the sternomastoid muscle and a complete dissection of the neck on that side. It is impossible to do a complete neck dissection without removing the internal jugular vein, and any one who tries it is in for a difficult operation. On the other hand, the radical neck dissection as outlined is a straightforward anatomic dissection. Few surgeons will agree on what constitutes a precancerous disease in the breast, yet we all agree that a lump in the breast should be removed to see if it is cancer. On the other hand, practically everybody agrees that the solitary nontoxic thyroid adenoma of the fetal type is a precancerous condition; therefore I think we should advise surgical excision of all such lesions.

SOME ROENTGENOLOGIC CONSIDERATIONS PERTAINING TO UPPER EXTREMITY PAIN

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It probably seems a bit odd and perhaps disappointing that a naval medical officer should deal with such a topic as upper extremity pain in times of war, when the fury of combat dominates the scene and the reek of gunpowder or trinitrotoluene fills the atmosphere. One would naturally expect or hope for a consideration of matters more specifically military.

In extenuation of my offense, I would like to point out that we can now afford less than ever to neglect the more prosaic and less glamorous fields of medical activity, for such neglect means the sapping of efficiency. The incidence of pain and disability involving the upper extremity is fairly high—just how high is difficult to say, since many cases are treated in an outpatient status and are not reflected in vital statistics with any approach to full measure. Many of these patients are seriously handicapped, are thoroughly miserable and at the same time have important duties. With all this in mind, I hope you will not take my efforts amiss.

Not so very long ago the etiologic differentiation of pains involving the extremities and the spine was in a rather rudimentary state. The tendency was to herd practically all of them together under the broad coverage of that ancient, patched and time worn umbrella—namely, rheumatism. The labor and studies of a generation or more of physicians has done much to clarify the situation and in latter years special advances have been made regarding the causes of low back pain and pain involving the lower extremities. I refer naturally to the discovery of the part played by disk injuries and hypertrophy of the ligamentum flavum; also misalinements especially at the lumbosacral articulation. These conditions have been thoroughly presented in numerous articles and textbooks. The matter of upper extremity pain, however, involves some conditions not so well clarified, and it appears well to take up a few of these from the standpoint of roentgenology.

Numerous indeed are the causes of the upper extremity pain, disability and abnormal sensation. A good many are of course obvious: contusions, sprains, fractures, dislocations, acute infections, rheumatic fever and the like. These seldom present diagnostic problems. Less obvious is the etiology in other cases, and naturally

Read before the Section on Radiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

increased recourse is had to radiography for aid in the diagnosis. From this group a large number will be easily and promptly separated as cases of so-called "bursitis" or, as frequently designated nowadays, paraarthritis or peritendinitis, depending on the preference of the roentgenologist as to terminology. The main thing is that in these cases calcium deposits are often noted near the shoulder joint in the soft tissues, usually just above the greater tuberosity of the humerus and mostly located in or about the supraspinatus tendon. The matter has been well presented in a number of articles, including one by Pinner and Staderman [1] and earlier in one by Sandström.[2] There is no need for further detail here. I should like only to remind you that pain and disability are often most exceedingly severe and that furthermore roentgen therapy is usually most efficacious, often in sensational fashion. This condition, be it remembered, is quite frequently encountered in the service and at times in comparatively young persons. It should always be borne in mind.

In a disappointingly large number of cases, however, we will find roentgenograms of the shoulder negative. In such case one does well not to shrug the matter off as just another perplexing case of neuralgia, neuritis, fibrositis, rheumatism or what not but to proceed further and have studies of the cervical spine and upper thorax made. In occasional cases one will find such things as tumors of the vertebrae, tumors of the cord and its membrane, superior sulcus tumors, infectious processes, more or less extensive synosteoses, possibly to the extent of the Klippel-Feil variety, anomalies of various types, and so on, not forgetting a possible ruptured disk and, what is fairly common, cervical ribs. However, it might be noted here that most cases of cervical ribs are found incidentally and appear to occasion symptoms only on more or less rare occasions. Now the differential diagnostics of the various unusual conditions is a very interesting and fascinating subject, but on this occasion I should like to come down to humbler, more everyday, fare and ask your attention to the troublesome matter of symptoms referable to changes in the vertebrae and thinning of the intervertebral disks consequent on arthritic changes of degenerative hypertrophic type. These are well worthy of particular consideration, if for no other reason than that the relationship of the symptomatology in these cases to the underlying pathologic condition and also to possibilities of therapy do not appear generally to be realized or else tend to be forgotten.

As mentioned by Mettier and Capp [3] in a study on neurologic symptoms in cervical arthritis, relationship between pain in the upper extremity and cervical arthritis was described some years ago by von Bechterew, Strümpell, Marie and others. These early writers noted, moreover, that there was little relation between the symptoms and the degree of arthritic involvement. It does not appear that much attention was paid to these observations then or, indeed, later. It seems that most of us tend to think of cervical arthritis as a remote and unlikely cause of upper extremity pain. On the contrary, it is a fairly frequent cause and the mechanism has been thought to involve the factors of narrowing of the intervertebral foramens due to productive osteoid changes and thinning of one or more disks, with irritation of or pressure on nerve roots. An explanation of the lack of correspondence between the degree of hypertrophic changes and the severity of symptoms becomes possible thereby: Arthritic changes of productive type need not and frequently do not affect the intervertebral foramens. If they are limited to the body margins they are relatively painless. In fact Oppenheimer and Turner [4] in their study on discogenic disease and segmental neuritis have placed all emphasis on disk narrowing. I myself feel that either narrowing of the disk or productive changes significantly located may be factors. In addition I would suggest that there may well be factors of round cell infiltration, passive congestion and perhaps some degree of fibrosis; in other words, that there is often some degree of chronic inflammation, and I believe that this factor may often be more important than osteoid proliferation and thinning of the disks.

As for treatment, Mettier and Capp mentioned that some victims were relieved to some extent by the manipulations of irregular practitioners; also that in general the syndrome has been inadequately treated. The patients, bewildered and discouraged, only too often drift from one physician to another and from clinic to clinic, obtaining little if any relief. Treatment recommended by Mettier and Capp is along the conventional lines of massage, manual traction and manipulation. This, they say, has relieved the majority of the patients. At the present time I believe that the most frequently applied remedy, aside from strictly medical measures, is diathermy. My own experience with diathermy indicates that it has been of little value in these conditions; indeed, it often seems to aggravate symptoms. Careful manipulation, traction and massage produce much better results and, finally, excellent results are to be expected from roentgen therapy if earnestly followed.

Coming to my own experience, I am not able to furnish a large statistical series chiefly because, as usually happens in naval practice, we lose track of too many of our patients. However, I have seen perhaps a hundred or so of such cases, and these enable me to come to certain conclusions: (1) These cases are frequently encountered; (2) they are quite resistant to the usual medical methods of treatment; (3) diathermy is seldom helpful, but, as already mentioned, other physical therapy procedures are; (4) treatment by x-rays is one of the most effective methods we have.

This brings me to the matter of a more detailed consideration of roentgen therapy and naturally to the manner in which this type of radiation operates to relieve symptoms and effect any curative benefits. People in general appear mystified and skeptical that anything might be expected from this form of therapy.

It is often noted in cases of peritendinitis that calcium deposits, particularly of the amorphous and less compact types, are absorbed after or during a course of x-ray therapy. However, relief of symptoms in these cases is nearly always extremely prompt, often within a few hours after the first irradiation; it is far in advance of any considerable absorption of calcium. Moreover, relief of pain occurs even when calcium deposits fail of any absorption. Thus we see that improvement is not dependent on melting away of calcium and that other factors must be concerned. Further, it is obvious that the roentgen ray is not apt to rebuild a thinned disk. These other factors, as I hinted before, are probably related to inflammation. As is now well known

1. Pinner, W. E., and Staderman, A. H.: Peritendinitis Calcarea, U. S. Nav. M. Bull. **39**: 521 (Oct.) 1941.
2. Sandström, C.: Peritendinitis Calcarea, Am. J. Roentgenol. **40**: 1 (July) 1938.
3. Mettier, S. R., and Capp, C. S.: Neurological Symptoms and Clinical Findings in Patients with Cervical Arthritis, Ann. Int. Med. **14**: 1315 (Feb.) 1941.
4. Oppenheimer, A., and Turner, E. L.: Discogenetic Disease of the Cervical Spine with Segmental Neuritis, Am. J. Roentgenol. **37**: 484 (April) 1937.

and has been well reviewed by Drs. Pendergrass and Hodes,[5] x-rays exert a potent beneficial effect on most inflammatory conditions. Although the exact details of the mechanisms involved are not too well understood, there appears to be more or less disintegration of white cells, particularly lymphocytes, with liberation of antibodies. However, changes in circulation likewise take place and, in fact, it is probably these changes which are of the most profound importance. Owing to the presence of an inflammatory reaction, we see infiltration by leukocytes, coagulation of lymph, appearance of fibroblasts and eventually formation of fibrous tissues in more chronic cases. All these tend to interfere with proper circulation and produce passive congestion. The effect of x-rays in appropriate dosage is to break up this type of reaction, which, although beneficial in walling off infected and damaged areas, none the less tends to be excessive, as only too often happens in natural processes. The end result of roentgen therapy is that an active circulation is substituted for passive congestion, thereby producing relief of pain and diminution in swelling along with encouragement of recovery. This relief of congestion is probably what accounts for the prompt relief of pain in so many cases, and of course it is the reactivated circulation which favors the absorption of calcium deposits. Naturally x-rays of themselves will not melt calcium.

Reverting to my cases of cervical arthritis and thinned disk, the main influence of x-rays doubtless is on the irritated and congested soft tissues about the affected segments. Reduction of swelling and improvement of circulation reduce the pressure on the nerve roots, and naturally symptoms improve. Any effect on the purely mechanical pressure from arthritic spurs or due to the thinned disks is not to be expected. It is notable too that the symptoms from these disorders of the cervical vertebrae are often slower to respond to x-rays than those from the so-called subdeltoid bursitis. Why this is so seems obscure, but the main thing is that they generally do respond in time and I usually caution these patients not to become discouraged if improvement is slow. Changes in the roentgenographic appearance of these cervical lesions have, in my experience, been negligible in contradistinction to the usual experience with shoulder calcification.

In connection with this form of therapy to the cervical spine it is interesting to note that hypertensive persons will commonly show a drop in blood pressure of substantial degree as the result of the effects of x-rays on the cervical sympathetic, chiefly the carotid ganglions. Unfortunately this improvement is not permanent.

As to plan of treatment and dosage employed, I have generally used moderate doses of 75 to 100 roentgens twice a week at first and later weekly. After six to eight treatments a rest period of about six weeks is given, followed by a second course. I have usually employed high voltage therapy (200 kilovolts, 0.5 mm. of copper and 3 mm. of aluminum filtration at 60 cm. distance). If this is not available a lower voltage with 3 mm. of aluminum or, better, 0.25 mm. of copper and 1 mm. of aluminum filtration will be usually found efficacious either in the cervical cases or in the cases in which the pathologic changes are limited to the shoulder proper.

As a word of caution it is necessary to point out that we are not going to help all cases and that accordingly if x-rays in adequate dosage fail to produce benefit we should desist and revert to the more usual methods, such as heat, massage, traction, manipulation and support. Naturally the usual medical approach is not to be overlooked in any case. As far as the roentgen ray is concerned, we must avoid either extremes of giving up before an adequate amount has been given (even up to 2,000 roentgens in stubborn cases) or, on the other hand, of persisting unduly in the face of poor response.

Before closing there is one more cause of upper extremity pain I should like to mention, and that is herpes zoster. Not infrequently there is a brachial distribution. The pain and discomfort from this disease surely need no emphasis. However, it should be emphasized and reemphasized that out of all the various remedies x-rays will generally do the most. Further, one has to remember that in elderly patients pain is likely to be unusually severe and resistant and that radiation therapy needs to be pushed with some persistence. These problems, I might add, are well considered by Drs. Carty and Bond [6] in a study on roentgen radiation as an analgesic agent.

SUMMARY

In many cases of pain and dysfunction involving the upper extremities, the roentgen ray will not only open the door to diagnosis but also frequently provide a most potent and welcome therapeutic agent.

5. Pendergrass, E. P., and Hodes, P. J.: Roentgen Irradiation in the Treatment of Inflammations, Am. J. Roentgenol. **45**: 74 (Jan.) 1941.

TOXIC REACTIONS TO THIOURACIL

REPORT OF CASES WITH ONE FATALITY

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The introduction of thiouracil in the treatment of thyrotoxicosis has occasioned renewed interest in the nonsurgical therapy of the disease. In 1941 Kennedy and Purves [1] observed that rapeseed and allyl thiourea were potent goitrogens. Subsequently the MacKenzies and McCollum [2] and Astwood [3] showed that thiourea and thiourea derivatives, especially 2-thiouracil, produced morphologic thyroid hyperplasia associated with inhibition of hormone production.

Astwood [4] first employed thiouracil in the treatment of patients with toxic goiter. This chemical compound is 2-thiouracil with the structural formula of NHCSNHCOCHCH. He found that the drug produced complete remission of symptoms and return of the basal metabolic rate to normal in most cases. These findings were confirmed by Williams and Bissell.[5] Our own experience is in accord with these reports.

6. Carty, J. R., and Bond, L. M.: Roentgen Radiation as an Analgesic Agent, Am. J. Roentgenol. **46**: 532 (Oct.) 1941.

From the Medical Service and Endocrine Clinic, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

1. Kennedy, T. H., and Purves, H. D.: Studies on Experimental Goiter: Effect of Brassica Seed Diets on Rats, Brit. J. Exper. Path. **22**: 241 (Oct.) 1941.

2. MacKenzie, Julia B.; MacKenzie, C. G., and McCollum, E. V.: Effect of Sulfanilylguanidine on the Thyroid of the Rat, Science **94**: 518 (Nov. 28) 1941. MacKenzie, C. G., and MacKenzie, Julia B.: Effect of Sulfonamides and Thiourea on the Thyroid Gland and Basal Metabolism, Endocrinology **32**: 185 (Feb.) 1943.

3. Astwood, E. B.; Sullivan, J.; Bissell, A., and Tyslowitz, R.: Action of Certain Sulfonamides and Thiourea on the Function of the Thyroid Gland, Endocrinology **32**: 210 (Feb.) 1943.

4. Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil, J. A. M. A. **122**: 78 (May 8) 1943.

5. Williams, R. H., and Bissell, G. W.: Thiouracil in the Treatment of Thyrotoxicosis, New England J. Med. **229**: 97 (July 15) 1943.

Early observations quickly showed the toxicity of thiouracil. Astwood,[6] reporting the first 30 cases of hyperthyroidism treated with the drug, noted 1 case of nonfatal agranulocytosis and 2 cases of drug fever. He felt that this 10 per cent incidence of toxic reactions might be due to excessive dosage. Williams and Bissell,[5]

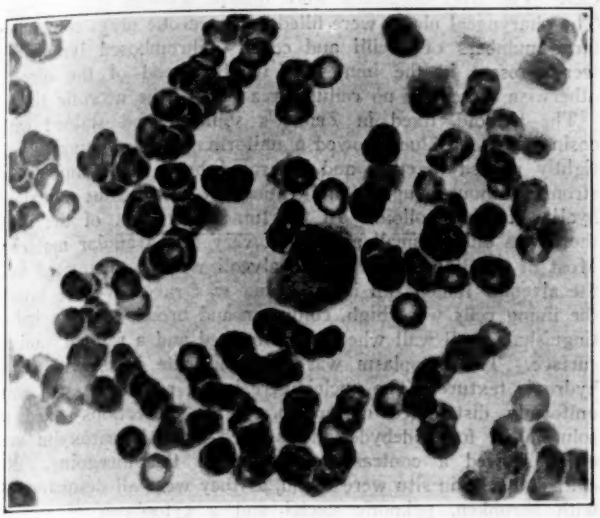

Fig. 1 (case 1).—Sternal marrow smear on April 18, 1944 at onset of agranulocytosis. Almost complete absence of white blood cells. One plasma cell is seen. Reduced from a photomicrograph with a magnification of 720 diameters.

in discussing complications of treatment, noted swelling and tenderness of the submaxillary salivary glands in 1 case. Gabrilove and Kert [7] described 3 cases with toxic manifestations in a total of 9 treated. One developed fever, lymphadenopathy and dermatitis; a second exhibited fever and dermatitis and a third showed moderate leukopenia.

Since February 1943 thiouracil [8] has been employed by us in the treatment of 43 cases of toxic goiter. The dosage employed has ranged from 0.1 to 1.0 Gm. daily. In this series of cases there have occurred the following toxic reactions: 1 fatal case of agranulocytosis, 2 cases of jaundice, 2 cases of drug fever and 2 cases of swelling of the submaxillary salivary glands. Also granulocytopenia occurred in a patient with severe heart failure who was given the drug in an attempt to produce myxedema.

AGRANULOCYTOSIS

CASE 1.—*History and Course.*—F. M., a white woman aged 56, a housewife, was admitted to the hospital on March 31, 1943 because of increasing fatigue and nervousness of seven months' duration and dyspnea, frequency of urination and weight loss of 25 pounds (11 Kg.) in the preceding three months. Frequent episodes of palpitation and trembling of the hands and knees had also occurred.

The patient was hyperactive, with staring, shiny eyes and flushed facies. The skin was moist and warm. There was widening of the left palpebral fissure but no other eye changes. There were fine tremors of the extended tongue and hands. The thyroid gland was symmetrically and diffusely enlarged to about twice the normal size. The pulse rate was 100 and the blood pressure was 110 systolic and 70 diastolic in millimeters of mercury. The weight was 123 pounds (56 Kg.).

The urine, blood cells, nonprotein nitrogen, sugar, cholesterol and serologic reaction showed no abnormalities. The basal metabolic rate was plus 30 per cent on admission.

The patient was given 0.6 Gm. of thiouracil for the first seventeen days, 0.4 Gm. for the next six days and 0.2 Gm. daily thereafter. The basal metabolic rate gradually fell until it was minus 2 per cent. The patient left the hospital on April 25, twenty-six days after entry. The symptoms and most of the signs of thyrotoxicosis had disappeared. The thyroid gland was smaller and softer, and the weight had increased steadily.

Following discharge from the hospital the patient was observed at weekly intervals in the Endocrine Clinic. At these visits the leukocyte count, basal metabolic rate, weight and pertinent clinical features were noted. The patient was maintained on 0.2 Gm. daily of thiouracil. Thirty days after the beginning of treatment her basal metabolic rate was minus 9 per cent and her weight 125 pounds (57 Kg.). The thyroid gland felt smaller and firmer. By the end of the second month of therapy the basal metabolic rate had dropped to minus 19 per cent and, although the patient was asymptomatic, puffiness of the eyelids had begun to appear. After ten weeks the basal metabolic rate was minus 18 per cent, the weight 134 pounds (61 Kg.) and the blood cholesterol 329 mg. per hundred cubic centimeters. The eyelids and face were puffy, and only the lower pole of the left thyroid lobe was palpable. After three months of therapy the patient complained of irritability and sluggishness. She showed considerable facial puffiness and a thick, dry skin. The basal metabolic rate was minus 24 per cent and the blood cholesterol was 367 mg. per hundred cubic centimeters. Thiouracil was omitted because of myxedema. The leukocyte count throughout the first three months had numbered between 6,400 and 10,500 per cubic millimeter, with abundant polymorphonuclear cells always present.

No thiouracil was administered for the subsequent four and one-half months. During this period the basal metabolic rate gradually rose to plus 9 per cent, the weight decreased 12 pounds (5.4 Kg.) and the patient developed mild symptoms of thyrotoxicosis. Thiouracil was readministered on October 15 in doses of 0.2 Gm. daily. After two weeks the basal metabolic rate had dropped to minus 4 per cent, the weight had increased

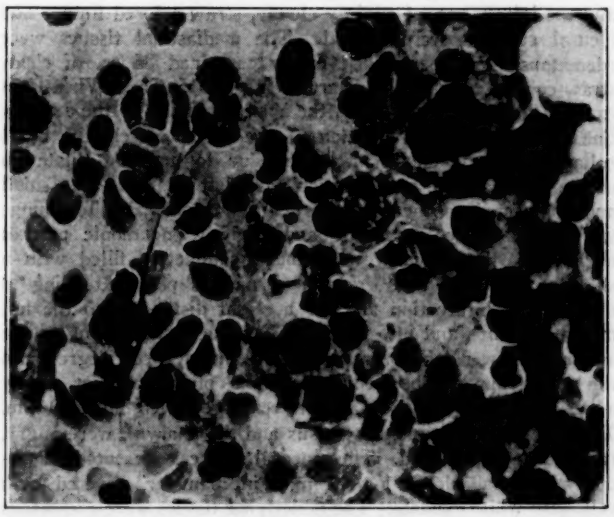

Fig. 2 (case 1).—Sternal marrow smear at necropsy. Myeloblasts and myelocytes are abundant. One neutrophil is seen at edge of field. Reduced from a photomicrograph with a magnification of 720 diameters.

by 2 pounds (0.9 Kg.) and her thyrotoxic symptoms had disappeared. At this time the thyroid gland was barely palpable. At the end of four weeks of the second period of thiouracil ingestion the basal metabolic rate was minus 13 per cent. At the end of eleven weeks the patient looked slightly myxedemic. The basal metabolic rate was minus 19 per cent and the blood cholesterol 312 mg. per hundred cubic centimeters. Thiouracil

6. Astwood, E. B.: Medical Treatment of Hyperthyroidism, Bull. New England M. Center **6**: 1 (Feb.) 1944.
7. Gabrilove, J. L., and Kert, M. F.: Sensitivity to Thiouracil, J. A. M. A. **124**: 504 (Feb. 19) 1944.
8. Supplied through the courtesy of Dr. B. W. Carey of the Lederle Laboratories.

was accordingly reduced in dosage to 0.1 Gm. daily. After twenty days on this dosage thiouracil was again omitted on Jan. 27, 1944 because of increasing signs and symptoms of myxedema. Three weeks later the basal metabolic rate had risen to plus 3 per cent and the patient felt and looked well. However, when the patient had not taken thiouracil for seven weeks mild thyrotoxic symptoms reappeared and the basal metabolic rate had risen to plus 21 per cent.

A third course of thiouracil in a dosage of 0.2 Gm. daily was accordingly begun on March 16, approximately one year after the initiation of treatment with the drug. Four weeks later, on April 15, the basal metabolic rate was plus 13 per cent and the patient still showed mild signs and symptoms of thyrotoxicosis. The leukocytes at this time numbered 6,500 per cubic millimeter. Thiouracil was continued in the same dosage.

The following day, April 16, the patient had new dentures fitted and noted pain and tenderness in the roof of her mouth. The next day, April 17, a sore throat developed followed by a severe, shaking chill and a temperature of 103.5 F. The patient appeared acutely ill, with flushed facies, gray coated tongue, large reddened tonsils covered with a grayish exudate and tender swollen lymph glands at the angles of the jaw. The leukocytes numbered 1,000 per cubic millimeter and the smear showed no polymorphonuclear cells. Thiouracil was omitted and the patient entered the hospital the next day. Treatment consisted of three blood transfusions, sodium sulfadiazine 5.0 Gm. and sodium sulfamerazine 9.0 Gm. intravenously, 270 cc. of pentnucleotide intramuscularly, liver extract and 150,000 units of penicillin. Ulcerations developed in the throat and tonsils. The white blood cells ranged between 900 and 1,650 per cubic millimeter. The hemoglobin was 11.3 to 12.5 Gm. per hundred cubic centimeters and the red blood cells averaged 4,000,000 per cubic millimeter. No polymorphonuclear cells appeared at any time, but on the day before death 1 myelocyte was seen in a count of 25 cells. Two sternal aspirations and bone marrow biopsies were done on the second and fourth days of hospital stay; both showed a hypoplastic marrow with granulocytic aplasia. The patient died suddenly on the sixth hospital day.

Postmortem Examination (Dr. M. J. Schlesinger).—Pertinent Gross Findings: The peritoneal cavity contained 500 cc. of slightly cloudy, straw-colored fluid. The surfaces were smooth and somewhat soggy. The right pleural cavity contained 400 cc. and the left 200 cc. of slightly cloudy, straw-colored fluid. The pleural surfaces were normal. The mediastinal tissues were edematous. The pericardial cavity contained 85 cc. of clear, straw-colored fluid. The heart weighed 315 Gm. When first exposed it seemed very large, the apex extending to the axillary line on the left. On incision of the blood vessels the heart collapsed, as the enlargement was due to manifest dilatation of the right auricle and ventricle; the left ventricle was small and contracted. Otherwise the heart was normal. The lungs were soft, flabby, atelectatic and free of pneumonic patches or edema. The trachea was almost completely filled with a slightly yellowish, clear, gelatinous mucoid plug extending to the tracheal bifurcation and for a slight distance into the left major bronchus and into the main branches of the right middle and right lower lobe bronchi, and to an advanced degree into the right upper lobe bronchus. The plug was not firmly adherent. The spleen was slightly enlarged, weighing 340 Gm. The base of the tongue, the tonsils and the pharynx were angry, raised and purplish red. The mucosal surfaces presented numerous superficial ulcers 1 to 2 mm. in diameter, covered with yellowish white exudate. The underlying tissues were edematous and congested. There were no pharyngeal abscesses and no laryngeal congestion or edema. Starting below the vocal cords a gelatinous plug was found in the trachea, similar in appearance to that found in the trachea and bronchi. There was a bilateral chain of enlarged cervical glands. The thyroid was about twice normal in size, uniform in texture and appearance and firm. The cut surface had a uniformly meaty, purplish red appearance. Embedded deeply in the left lobe was a small, light-colored nodule about 6 mm. in diameter. The bone marrow of the vertebrae, sternum, ribs and middle of the shaft of the left femur was examined. The femur marrow was yellow and fatty. Elsewhere the marrow was abundant, pasty and slightly brownish.

Pertinent Microscopic Findings: The lungs showed congestion without hemorrhage or edema, small areas of atelectasis and small emphysematous blebs. In the larger bronchi the epithelium was either desquamated or filled with mucous blebs. The splenic pulp was moderately congested, with small and inactive corpuscles. The liver sinusoids were dilated without cell necrosis. The pharyngeal ulcers were filled with necrotic plugs containing large numbers of bacilli and cocci. Thrombosed lymphatics were present in the immediate neighborhood of the ulcers; otherwise there was no cellular reaction to the necrotic tissue.

The thyroid, fixed in Zenker's solution and stained with eosin-methylene blue, showed a uniform picture of small acini, tightly packed together and separated by a small amount of stroma without lymphoid infiltration: a rare acinus contained hyaline-staining colloid. In the lumens of most of the acini there was only a small amount of very fine granular material. Most of the lining cells of the alveoli were desquamated into the alveolar lumen; an intact lining was rare. Where intact, the lining cells were high, columnar and broad, with an indistinguishable cell wall where they touched and a ragged luminal surface. The cytoplasm was thin and pale blue, with loose hydropic texture. The nuclei were large, round or oval, with uniformly distributed chromatin. Thyroid sections fixed in solution of formaldehyde and stained with hematoxylin and eosin showed a contrasting picture to the foregoing. No epithelial cells in situ were found, as they were all desquamated, with shrunken, pyknotic nuclei and a cytoplasm of stringy material attached to the nucleus. Two nodules were noted in one of the sections stained with hematoxylin and eosin; one enclosed in thick connective tissue, the second unencapsulated but clearly demarcated. The thyroid tissue in these nodules was composed of small acini, many containing colloid, and lined with fairly well preserved, low cuboidal cells in striking contrast to the cellular disintegration outside the nodule.

The bone marrow in the shaft of the femur was largely composed of fat with a few tiny islands of marrow cells. The sections from the ribs were at least half fat; the remainder consisted of marrow-forming cells. These nests of marrow cells were composed of an equal mixture of large undifferentiated cells with a bluish cytoplasm and of definite normoblasts. No eosinophilic myelocytes were found.

This patient with thyrotoxicosis was treated with three courses of thiouracil over a period of approximately one year. The first course of thiouracil, which lasted three months with an average daily dose of 0.2 Gm., was followed by the development of myxedema and a remission which lasted four and one-half months. The second course of thiouracil, with an average daily dose of 0.2 Gm., lasted fourteen weeks and was followed by the reappearance of myxedema and a remission which lasted seven weeks. In the third and final course the patient received a daily dose of 0.2 Gm. of thiouracil for four weeks, when agranulocytosis suddenly appeared, followed by death in six days in spite of transfusions, penicillin, sulfadiazine, sulfamerazine, liver extract and pentnucleotide. Postmortem examination showed extensive granulocytic hypoplasia of the marrow, ulcerative pharyngitis, an occluding tracheobronchial mucous plug, pulmonary congestion and atelectasis, and acute dilatation of the right auricle and ventricle. The thyroid gland showed alveolar hyperplasia and hydropic degeneration with absence of colloid and lymphocytic infiltration.

Case 2.—Granulocytopenia with dermatitis. J. S., a white man aged 57, an upholsterer, with a previous admission four months earlier for congestive heart failure, entered the hospital on Sept. 3, 1942 because of severe angina pectoris and heart failure unimproved by adequate digitalization and bed rest. The patient was dyspneic, orthopneic and cyanotic. The neck veins were engorged. The heart was enlarged downward to

the left and had a loud mitral systolic murmur. There were medium moist rales over both lung bases. The liver was enlarged to four fingerbreadths below the right costal margin; ascites and moderate ankle edema were present. The blood pressure was 140 systolic and 110 diastolic. Urinalyses showed specific gravities ranging between 1.010 and 1.020 (uncorrected for albumin), heavy traces of albumin, no sugar and varying numbers of red and white cells, with occasional hyaline and granular casts in the sediment. The blood nonprotein nitrogen varied between 45 and 64 mg. per hundred cubic centimeters. The blood cholesterol varied between 404 and 500 mg. per hundred cubic centimeters. The blood carbon dioxide combining power was 46 volumes per cent. The total protein of the serum ranged between 5.97 and 7.46 Gm. per hundred cubic centimeters with a normal albumin-globulin ratio. Numerous electrocardiograms showed normal rhythm with defective intraventricular conduction, left axis deviation and prominent Q waves in leads 1, 2 and 3. Hematologic examination showed a hemoglobin value of 110 per cent (15.95 Gm.), erythrocytes numbering 5,600,000 per cubic millimeter and leukocytes numbering 7,900 per cubic millimeter, with 64 per cent polymorphonuclear leukocytes, 34 per cent lymphocytes and 2 per cent monocytes. Roentgenologic examination of the chest showed a hypertensive heart with pronounced congestive changes in the lungs.

Despite the reduction in dosage leukopenia continued, and three days later the leukocytes numbered 2,100 per cubic millimeter with 7 per cent neutrophils, 72 per cent lymphocytes and 21 per cent monocytes. The hemoglobin dropped to 90 per cent (13.05 Gm.) and the erythrocytes dropped to 4,000,000 per cubic millimeter. Thiouracil was omitted, a transfusion with 750 cc. of whole blood was given and pentnucleotide 40 cc. administered daily. The following day the leukocytes numbered 3,300 per cubic millimeter with 11 per cent neutrophils, 68 per cent lymphocytes and 20 per cent monocytes. Thereafter there was a steady increase in the neutrophil percentage and total white count, so that by the end of six days the total white count was 6,700 per cubic millimeter with 64 per cent neutrophils, 29 per cent lymphocytes and 7 per cent monocytes, as shown in the table.

Three days after leukopenia had developed urticaria appeared, first over the right wrist, progressing in the next two days to involve the lower lip and eyes. These skin manifestations disappeared after omission of the drug.

Throughout the period of granulocytopenia the patient was afebrile except for a single temperature rise to 101.4 F. Pruritus, associated with the urticaria, was the only symptom noted. No change in the basal metabolic rate occurred as a result of the administration of thiouracil. The patient was discharged from the hospital on Oct. 31, 1942.

Hematologic Observations Before, During and After Thiouracil (Case 2)

Date	Thiouracil, Daily Dose, Gm.	White Blood Cells, Cu. Mm.	Polymorphonuclears, %	Lymphocytes, %	Monocytes, %	Eosinophils, %	Basophils, %	Hemoglobin, %*	Red Blood Cells Cu. Mm.	Comments
9/20/42	0	7,900	64	34	2	0	0	110	5,600,000	Initial values
9/26/42	0.8	8,000	75	23	2	0	0	112	5,150,000	Thiouracil started 9/25/42
10/ 1/42	0.6	9,300	61	31	3	4	1	114	5,900,000	
10/19/42	0.4	3,300	32	50	17	0	1	104	5,250,000	Thiouracil 25th day
10/20/42	0	.....	..	..	..	..	..	106	5,250,000	Thiouracil omitted; urticarial dermatitis
10/21/42	0	2,100	7	72	21	0	0	92	4,000,000	500 cc. whole blood; pentnucleotide 40 cc.
10/22/42	0	3,300	11	68	20	0	0	...	.....	250 cc. whole blood; pentnucleotide 40 cc.
10/23/42	0	3,800	36	54	10	0	0			
10/24/42	0	5,300	60	35	5	0	0			
10/25/42	0	3,700	43	46	10	0	1	90	4,650,000	
10/26/42	0	6,700	64	29	7	0	0			
10/27/42	0	8,300	64	29	6	0	1			

* Based on 100% = 14.5 Gm.

The patient was treated with bed rest, a low salt diet, digitalis, diuretics and glyceryl trinitrate. Since this regimen did not materially benefit his angina pectoris or adequately control his heart failure, and because of previous prolonged disability from heart failure, total thyroidectomy was considered. Because of impaired renal function, this procedure was not undertaken and an attempt to produce myxedema by the use of thiouracil was substituted. The basal metabolic rate was first determined and found to range between plus 9 and plus 18 per cent in a series of five determinations. This elevation was due to heart failure, as the blood velocity measurements (arm to tongue) were prolonged to an average of 35 seconds and the venous pressure increased to an average of 15 cm.

The drug was started on September 25 in doses of 0.8 Gm. daily. At this time his erythrocytes were 5,150,000 per cubic millimeter, hemoglobin 112 per cent (16.2 Gm.) and leukocytes 8,000 per cubic millimeter with 75 per cent neutrophils, 23 per cent lymphocytes and 2 per cent monocytes. After seven days the dose of thiouracil was reduced to 0.6 Gm. daily. At this time the hemoglobin was 114 per cent (16.5 Gm.), the erythrocytes were 5,900,000, and the leukocytes were 9,300 per cubic millimeter with 61 per cent neutrophils, 31 per cent lymphocytes, 3 per cent monocytes, 4 per cent eosinophils and 1 per cent basophils. After eighteen days the dosage was again reduced to 0.4 Gm. daily because on the preceding day the leukocytes were found to number 3,300 per cubic millimeter with 32 per cent neutrophils, 50 per cent lymphocytes, 17 per cent monocytes and 1 per cent basophils. The hemoglobin was 104 per cent (15.1 Gm.) and the erythrocytes numbered 5,250,000 per cubic millimeter.

He reentered the hospital on Feb. 10, 1943 because of recurrence of heart failure. Therapy with bed rest, diet, digitalis and diuretics was unavailing and the patient died on April 29. Postmortem examination showed aneurysm of the left ventricle, coronary sclerosis, left ventricular hypertrophy, bronchopneumonia, bronchiectasis, a bronchiectatic cavity with small lung abscesses, chronic glomerulonephritis and chronic passive congestion. The thyroid gland was entirely normal on gross and microscopic examination. The bone marrow was also normal, showing active formation of red and white blood cells.

This patient with chronic heart failure and angina pectoris was given thiouracil in doses of 0.8 Gm. daily for six days, 0.6 Gm. daily for eighteen days and 0.4 Gm. daily for two days. On the twenty-fifth hospital day he developed leukopenia and neutropenia and on the twenty-seventh day severe neutropenia associated with slight reduction in the hemoglobin values and red blood cell count. At this point the drug was omitted. An urticarial dermatitis appeared simultaneously with the onset of the neutropenia. Complete recovery ensued, following treatment with transfusions and pentnucleotide.

JAUNDICE

CASE 3.—R. F., a white woman aged 54, a housewife, entered the Beth Israel Hospital on May 12, 1943 because of increasing dyspnea, orthopnea, substernal pain, weakness and a weight loss of 16 pounds (7.3 Kg.) in the preceding three months. Three years previously the patient had been hospitalized for

hypertensive heart disease. On examination the patient showed orthopnea, a warm moist skin, moderate exophthalmos, distended neck veins and moderate diffuse enlargement of the thyroid gland. The heart was considerably enlarged downward and to the left, with a loud systolic murmur in the second left interspace and regular rhythm; the blood pressure was 230 systolic and 90 diastolic. The lung bases showed a few fine rales; there was no enlargement of the liver or peripheral edema. Urinalyses were uniformly negative. The leukocytes, erythrocytes and hemoglobin values were within the normal range. The blood nonprotein nitrogen was 30 mg. per hundred cubic centimeters. The electrocardiogram showed the pattern of chronic left ventricular strain. The arm-to-tongue circulation time (calcium gluconate) was 15 seconds. The basal metabolic rate was plus 64 per cent initially and in a repeated determination four days later.

On May 23 auricular fibrillation developed and the patient was digitalized. Because of the elevated basal metabolic rate and the clinical signs of thyrotoxicosis, Lugol's solution was administered on May 25. Six days later the basal metabolic rate was plus 31 per cent. On June 5 the basal metabolic rate was plus 25 per cent. On June 9 the basal metabolic rate was plus 30 per cent and on June 22 it was plus 17 per cent. Because of a persistently normal pulse rate, averaging 70 per minute at all metabolic levels, and despite the good clinical and metabolic response, Lugol's solution was omitted in order conclusively to establish the diagnosis of thyrotoxicosis. The patient was discharged on June 30 and was thereafter followed in the Endocrine Clinic. Maintenance doses of digitalis were continued. Approximately one month later the patient developed aggravation of the thyrotoxicosis with an increase in the basal metabolic rate to plus 48 per cent. Iodine was therefore readministered in the form of saturated solution of potassium iodide, 10 drops daily, and reduced the basal metabolic rate to plus 33 per cent after three weeks. Because the patient was not clinically improved, thiouracil 0.8 Gm. daily was added on August 13. One week later the basal metabolic rate was plus 25 per cent and there was noticeable improvement. Thiouracil was reduced to 0.6 Gm. daily and after two weeks, on September 3, the basal metabolic rate was plus 28 per cent, but the patient complained of generalized itching. On examination there were multiple linear scratch marks and questionable scleral icterus. Because a dermatologic consultant felt that scabies was the cause of the

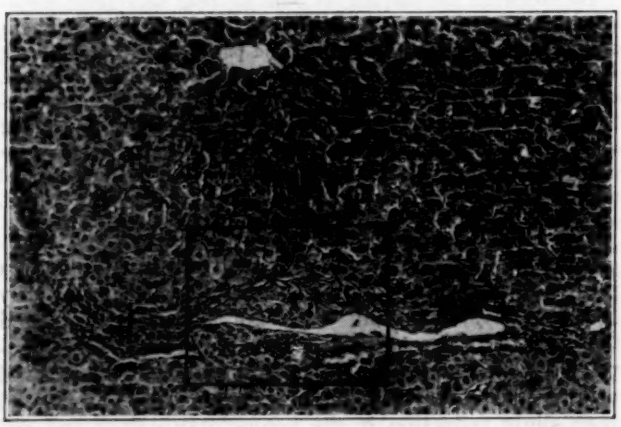

Fig. 3 (case 3).—Section of liver. Dilated central vein, normal hepatic cells, clearly defined and empty sinusoids. Cellular infiltration about the portal area. Bile thrombi and distended bile capillaries not clearly apparent at this magnification. Reduced from a photomicrograph with a magnification of 180 diameters.

pruritus, thiouracil was continued in the same dosage. Within the next week the patient noted diarrhea, dark urine and clay-colored stools, and continued severe pruritus. There was no abdominal pain, epigastric distress, nausea, vomiting or colic. On examination there was deep generalized icterus without enlargement of the liver or spleen. Thiouracil was omitted and the patient reentered the hospital on September 13.

During the next ten days there was increasing jaundice with a rise in the icterus index from an initial value of 85 to 180. The stools were clay colored. The urine contained large amounts of bile and no urobilin. The patient experienced one episode of upper abdominal pain, colicky in nature, of one hour's duration. Except for pruritus and nausea the patient was otherwise asymptomatic. Radiographic examination of the chest and gastrointestinal tract gave normal results. The galactose

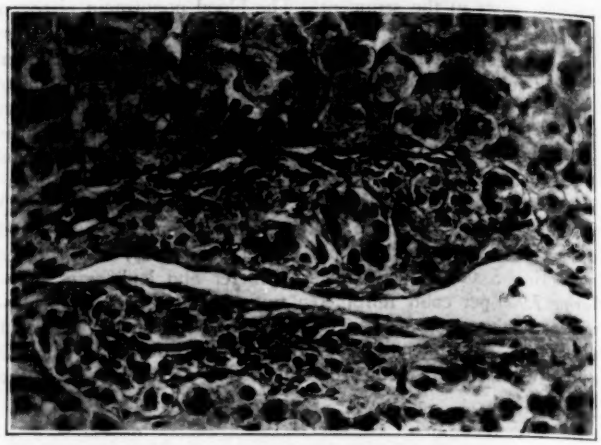

Fig. 4 (case 3).—Section of liver. Magnification of window in figure 3. Normal hepatic cells, periportal cellular infiltration. Large bile ducts with open lumens clearly visible. Reduced from a photomicrograph with a magnification of 720 diameters.

tolerance test, blood urea concentration, blood total protein and albumin-globulin ratio, blood cholesterol and cholesterol esters were normal. The alkaline phosphatase of the blood was 16 units (Bodansky). The basal metabolic rate was plus 35 per cent and plus 29 per cent on two occasions.

Since the jaundice appeared obstructive in nature, laparotomy was done on September 24. At operation the gallbladder was thin walled, normal in appearance and free of palpable stones. The common duct was thin, soft and nondistended. Aspiration revealed dark, clear bile containing no sediment. The pancreas felt normal. Biopsy of the liver was taken and the operation was terminated. Common duct exploration and cholangiography were not performed. The liver was shrunken and green.

The microscopic examination of the liver showed prominent central veins and normal parenchymal cells. The sinusoids were clearly demarcated and empty, well lined with prominent Kupffer cells. The bile capillaries between the cells of the liver cords were manifestly distended. Those in the outer half of the lobule were distended but empty, while those in the inner half of the lobule were distended and plugged with yellow-green bile pigment. In the portal areas the larger bile ducts were empty but showed evidence of recent distention by the prominence of their open lumens. The portal areas were infiltrated with some mononuclear and rare polymorphonuclear cells. The histologic picture described is that usually associated with acute bile stasis.

Following operation the jaundice gradually lessened and bile appeared in the stool on the fourth postoperative day. The patient left the hospital on October 15 with an icterus index of 33; the index finally became normal on December 10. The total duration of jaundice was one hundred days.

Throughout her hospital stay the patient received iodide medication and this was continued during her supervision in the outpatient department. The basal metabolic rate gradually rose, in spite of iodine, from plus 23 per cent to plus 54 per cent, with increasing signs of thyrotoxicosis. A second trial with thiouracil was therefore begun on Feb. 11, 1944. Extreme dizziness and weakness developed on that day, after she had taken 0.6 Gm. of thiouracil in divided doses. On the following day she took 0.8 Gm. and developed itching of the extremities and diarrhea. She felt feverish and drowsy and perspired excessively on these two days. Thiouracil was omitted. She

was not seen in the clinic until February 16, at which time no jaundice was apparent; the leukocyte count on that day was 7,850 per cubic millimeter with abundant polymorphonuclear cells.

Subsequently the patient was treated with potassium iodide alone and underwent thyroidectomy on March 13. Because of operative injury to the recurrent laryngeal nerve, only hemithyroidectomy was performed. The thyroid histologically showed hyperplasia and involution. Mild thyrotoxicosis has persisted since this operation and has been controlled with iodine.

This 54 year old woman with hypertensive heart disease and toxic diffuse goiter developed severe jaundice three weeks after the administration of thiouracil in doses of 0.6 to 0.8 Gm. daily. Omission of the drug failed to alleviate the jaundice, which in fact increased until the icterus index was 180. Because the jaundice appeared obstructive in nature, laparotomy was performed, with the finding of a normal gallbladder and common bile duct. The liver biopsy, however, showed the histologic picture of acute bile stasis without hepatitis. The jaundice disappeared after one hundred days. Readministration of thiouracil for two days produced toxic symptoms. Thyroidectomy was eventually performed for the control of the thyrotoxicosis.

CASE 4.—J. B., a man aged 30, a shipyard worker, entered the hospital on June 7, 1944 complaining of nervousness, tremors, diarrhea, palpitation, increased irritability and hyperhidrosis of two months' duration. He had lost 15 pounds (6.8 Kg.) in spite of a good appetite. On examination he appeared hyperactive, with a warm, moist skin and tremors of the tongue and hands. The eyes were staring but otherwise normal. The thyroid was diffusely enlarged to twice normal size and felt firm. The heart had a forceful apex impulse but was not enlarged and showed a regular rhythm at a rate of 120. Both breasts were moderately enlarged, nodular and tender. The blood pressure was 120 systolic and 70 diastolic.

Four urine analyses were negative. Hematologic studies were normal. The fasting blood sugar was 103 mg. per hundred cubic centimeters and the blood cholesterol was 294 mg. per hundred cubic centimeters. The basal metabolic rate on June 8 was plus 59 per cent and on June 9 was plus 54 per cent.

On June 8 thiouracil 1.0 Gm. daily was administered and continued in that dose until June 15, when it was reduced to 0.6 Gm. daily. On that day the basal metabolic rate was plus 11 per cent and the patient left the hospital. Clinical improvement occurred coincidentally with the lowering of the basal metabolic rate. The thyroid decreased in size and became softer.

The patient continued to take 0.6 Gm. daily of thiouracil for the next fifteen days. When seen on June 30 he was free from all symptoms and signs of thyrotoxicosis and stated that he had been doing full time work since June 20. His basal metabolic rate was minus 14 per cent, with a pulse rate of 80. The leukocyte count was 5,400 per cubic millimeter, with a normal differential count. Thiouracil was reduced to 0.4 Gm. daily.

Three days later, on July 3, pruritus of the extremities, without dermatitis, developed and thiouracil was stopped. The following day clay-colored stools and dark urine were noted and there was increased pruritus. On July 5 the patient was moderately jaundiced, with bilirubinuria and an icterus index of 18. The leukocyte count was 12,150 per cubic millimeter. Saturated solution of potassium iodide was begun on that day and has been continued to the present. By July 7 the pruritus had ceased, although the stools remained acholic until the next day, when the icterus index was 15. Bilirubinuria, without urinary urobilin, continued until July 11. On July 21 the icterus index was still elevated to a level of 16, although by this date the stools contained bile; the urine was bile free and contained urobilin. The basal metabolic rate on this date was minus 5 per cent, and the leukocytes numbered 6,500 per cubic millimeter. The patient was asymptomatic. The icterus index returned to normal on July 31.

This 30 year old patient with thyrotoxicosis and gynecomastia developed symptoms and signs of obstructive jaundice following the administration of thiouracil for twenty-four days. The pruritus disappeared four days after omission of the drug, but the icterus index remained elevated for twenty-six days. Thiouracil was not readministered, as in case 7, to prove the etiologic relationship, but the coincidental occurrence of catarrhal jaundice in this case seems adequately excluded by the fairly prompt recovery following omission of the drug.

DRUG FEVER

CASE 5.—J. B., a white woman aged 60, a housewife, with a history of toxic goiter in 1 brother and a past history of nodular nontoxic goiter treated at another hospital by a right hemithyroidectomy in 1939, was admitted to the Beth Israel Hospital on Nov. 29, 1943 because of palpitation, nervousness, easy fatigability, sleeplessness, diarrhea and sweating of three months' duration. During this period she had lost 15 pounds (6.8 Kg.) in weight.

The menopause had occurred ten years previously, and since then she had had mild hypertension. She had borne five children, all of whom were alive and well except for one daughter with diabetes.

The patient was an alert, jumpy woman with flushed facies, shiny eyes and warm moist skin. There was no exophthalmos or lid lag. There was a hair line thyroidectomy scar. The left lobe of the thyroid was three times the normal size; the right lobe was not felt. The extended hand showed a fine tremor. The heart rate was 120 and the blood pressure was 160 systolic and 76 diastolic.

Examination of the blood and urine showed no abnormalities. The leukocytes ranged between 6,150 and 9,650 per cubic millimeter and neutrophils averaged 75 per cent. The fasting blood sugar was 77 mg. per hundred cubic centimeters and the blood cholesterol was 171 mg. per hundred cubic centimeters. The basal metabolic rate was plus 38 per cent on November 30 and plus 35 on December 1.

Thiouracil was started on December 1 in doses of 1.0 Gm. daily. During the ensuing three days striking aggravation of symptoms and signs occurred, the patient complaining of palpitation, weakness and restlessness and showing an increase in pulse rate and in skin hyperemia. On December 4 improvement began to appear, and on the 7th the basal metabolic rate had dropped to plus 15 per cent and the pulse rate to 105. Thiouracil was decreased to 0.6 Gm. daily.

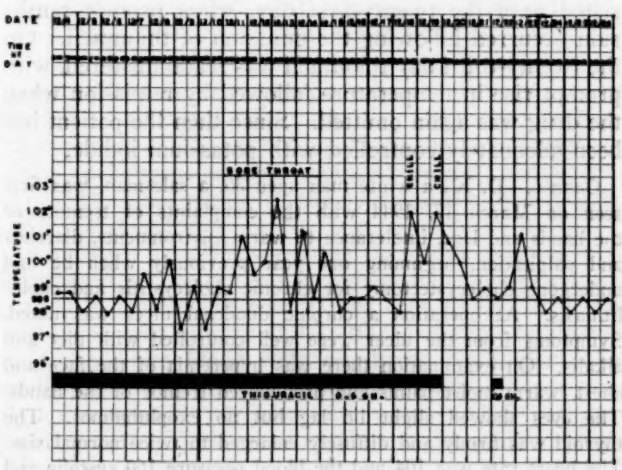

Fig. 5 (case 5).—Febrile reaction to thiouracil. Following subsidence of fever due to sore throat, note drug fever accompanied by chill on December 18 and 19, with defervescence on omission of drug and recurrence of fever with readministration.

On December 11 the patient complained of sore throat. Her temperature rose to 101 F. and her pulse rate to 130. The throat showed diffuse bright redness throughout the fauces and pharynx. The throat culture showed weakly hemolytic strepto-

cocci. The leukocyte count was 6,800 per cubic millimeter, with 76 per cent neutrophils. She was treated with acetylsalicylic acid and hot saline throat irrigations. Thiouracil was continued in the same dosage. The throat symptoms improved steadily during the following four days, and the temperature was normal on December 15.

On the evening of the 18th the patient had a chill and her temperature rose to 102 F. She complained of headache, general malaise and restlessness. Physical examination revealed no cause for this change in the patient's condition. The leukocyte count was 9,300 per cubic millimeter, the urine showed no abnormalities and a blood culture showed no growth of any organisms. The next morning the temperature rose to 102 F. The patient complained of headache and of generalized aches and pains and was restless. The leukocyte count was 9,600 per cubic millimeter and the physical examination remained negative. The fever persisted during the following day and the patient continued to have headache. Thiouracil was omitted on December 21, whereupon the temperature promptly dropped to normal, and the patient felt better.

The basal metabolic rate on December 23 was plus 10 per cent. On the following day thiouracil was again administered. After the second dose of 0.2 Gm. the temperature rose to 101 F. and the patient complained of restlessness, headache and nausea. Thiouracil was stopped and the temperature promptly dropped.

Despite omission of thiouracil, improvement in the thyrotoxicosis continued. The basal metabolic rate on December 27 was ± 0, and the patient was discharged without further administration of thiouracil.

This patient, with toxic diffuse goiter and mild arterial hypertension, showed an initial aggravation of signs and symptoms following the administration of thiouracil. In spite of this the drug was continued, and after one week striking clinical and metabolic improvement had occurred. On the eleventh day of drug administration she developed a streptococcic sore throat associated with fever and a normal leukocyte count. By the fifteenth day she had recovered from this episode. On the eighteenth day chills and fever developed and persisted until the twenty-first day, when prompt remission occurred following the omission of thiouracil. On the twenty-third day thiouracil was readministered, with prompt rise in temperature followed by remission when the drug was again omitted. Since then the patient has been adequately controlled with potassium iodide.

Case 6.—D. K., a white man aged 36, a salesman, was first seen on March 17, 1944 with the complaints of tremors of the hands and legs, intolerance to warm environments, diarrhea and palpitation, beginning one year previously when he had undergone cholecystectomy for chronic cholecystitis and cholelithiasis. At operation a chronic duodenal ulcer was noted. Symptoms from the ulcer were well controlled with diet and alkalis. On examination there was hyperemia of the face and chest, warm moist palms and pronounced tremor of the hands. The eyes showed slight lid lag but no exophthalmos. The thyroid was firmly and diffusely enlarged to twice normal size. The heart rate was 104 and the blood pressure 160 systolic and 70 diastolic. The examination of the urine showed no abnormalities. The leukocyte count was 7,500 per cubic millimeter, with 60 per cent neutrophils. The basal metabolic rate on three occasions was plus 50, 49 and 49 per cent.

Thiouracil was started on March 24 in doses of 1.0 Gm. daily. One week later the basal metabolic rate was plus 34 per cent, the pulse rate 84 and the leukocyte count 8,400 per cubic millimeter. Thiouracil was continued in the same dosage. On the ninth day of therapy the patient developed a choking sensation in the throat and chest, nausea and vomiting, and temperature elevation to 102 F., with copious sweating and generalized aches and pains. This continued on the tenth day, when thiouracil was omitted with prompt defervescence and remission of symptoms. Examination on the eleventh day showed no change in the patient's signs, except that the blood pressure was 130/70 and the weight had increased 4 pounds (1.8 Kg.). The leukocytes numbered 8,600 per cubic millimeter and the hemoglobin was 100 per cent (14.5 Gm., Sahli). Thiouracil was readministered in doses of 0.6 Gm. daily on the eleventh day. One hour after 0.2 Gm. had been taken, burning of the eyes and a temperature rise to 99.0 F. occurred. The patient, however, continued to take the thiouracil on that day and one hour after 0.6 Gm. had been taken he developed choking sensations in the throat, chilliness, a persistent nonproductive cough, severe burning of the eyes, dyspnea and a fever of 102.5 F. The fever and symptoms persisted all night. Examination on the twelfth day showed evident conjunctival injection and moderate splenomegaly. The leukocyte count was 9,000 per cubic millimeter with 60 per cent polymorphonuclear cells, 12 per cent lymphocytes and 18 per cent monocytes. The red blood cells and platelets appeared normal. Thiouracil was omitted, and prompt remission of symptoms occurred.

On the thirteenth day the daily administration of 10 drops of saturated solution of potassium iodide was begun. On the sixteenth day the patient was admitted to the Beth Israel Hospital. At this time the temperature was normal, pulse rate 92 and the blood pressure 125 systolic and 65 diastolic. There were fine tremors of the hands, slight lid lag, diffuse firm enlargement of the thyroid and a palpable spleen. The basal metabolic rate was plus 10 per cent. The hemoglobin was 112 per cent (17.4 Gm.), the red blood cells numbered 5,400,000 and the white blood cells 11,900 per cubic millimeter, with 55 per cent neutrophils, 38 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. Four urine examinations revealed no abnormalities.

Medication with potassium iodide was continued, and on April 21 subtotal thyroidectomy was performed because of incomplete control of thyrotoxicosis with iodine. The splenomegaly had disappeared by the time of operation.

The operation was performed after the patient had received iodine for nineteen days and twenty-three days after the omission of thiouracil. Microscopic examination of the thyroid showed areas of extensive hyperplasia and accentuated hyperinvolution with lymphoid tissue scattered about in small and large groups, often containing germinal centers.

Following operation the patient's recovery was uneventful. One month postoperatively the basal metabolic rate was minus 8 per cent, with a pulse rate of 66.

This second case of drug fever caused by thiouracil developed on the ninth day of administration. The causal relationship to thiouracil was proved by readministration of the drug. In this case there were definite constitutional reactions, splenomegaly and monocytosis.

SUBMAXILLARY SALIVARY GLAND SWELLING

Case 7.—A. G., a white man aged 59, a carpenter, with toxic nodular goiter and auricular fibrillation, developed a painful, egg-sized swelling of both submaxillary salivary glands after one month of thiouracil medication with a daily dose of 0.4 Gm. He showed a temperature rise to 99.8 F. and a leukocyte count of 15,000 per cubic millimeter at the height of the swelling. The drug was continued in the same dosage, but he was kept in bed and fluids were forced. One week later there was decided reduction in the size of the glands and absence of tenderness. After two weeks the submaxillary glands were impalpable. There was no recurrence of this complication despite continuation of thiouracil for over six months.

Case 8.—M. K., a woman aged 28, a housewife, with toxic diffuse goiter, developed painful, moderate sized swelling of both submaxillary salivary glands after one month of thiouracil medication with a daily dose of 0.4 Gm. No fever or leukocytosis occurred. Although thiouracil was continued, the swelling subsided and did not recur during subsequent administration of the drug over a period of several months.

COMMENT

Before utilizing thiouracil in the treatment of toxic goiter in man, Astwood [9] investigated the chemical nature and toxic effects of antithyroid substances and found well defined individual variations in toxicity as well as in antithyroid effect. Thiourea and thiouracil were low in toxicity and active in depressing thyroid function. Of thiouracil he noted that "when this compound was fed at a level of 1 per cent in the food [of rats], concretions in the urinary tract were noted in about one third of the animals." Subsequently Williams [10] found a few instances of distinct leukopenia and anemia in rats receiving thiouracil, although bone marrow sections were normal.

The toxic manifestations of thiouracil in animals gave little clue to the range of harmful effects which were later observed in man. When these effects began to appear, the dosage of the drug or idiosyncrasy was implicated as an etiologic factor. Astwood [4] early warned that thiouracil might prove to be disadvantageously toxic as compared with thiourea. However, thiourea, with a very simple formula (NH_2CSNH_2) and the basic drug of the thiourea group of antithyroid substances, has already proved seriously toxic. Because of its unpalatability it has not received extensive trial; nevertheless Astwood [6] noted a skin rash in several instances, and Newcomb and Deane [11] noted severe granulocytopenia and thrombocytopenia in a patient with toxic goiter who had received the drug over a period of five weeks.

Thiouracil has been reported to produce the following toxic effects in man: agranulocytosis and granulocytopenia, drug fever, varied types of dermatitis, swelling of the submaxillary salivary glands, arthritis and arthralgia, edema of the legs and nausea with vomiting. The incidence of these complications has been between 10 and 20 per cent.

Jaundice.—To the preceding list of complications we add jaundice, which was encountered twice in our series. In both instances this complication occurred during the second or third week of drug administration. The jaundice had the clinical and laboratory characteristics of obstructive jaundice. Laparotomy in 1 case, however, showed no extrahepatic biliary tract obstruction, but liver biopsy revealed evident biliary stasis and pericholangitis with normal liver parenchyma. These clinical and pathologic findings resembled in every detail the syndrome of postarsphenamine jaundice apparently due to obstruction of the intrahepatic biliary tract, first described by Hanger and Gutman.[12] In their 12 cases it is noteworthy that the hepatotoxic reaction developed after the second or third intravenous arsenical injection. Jaundice appeared within several days and persisted for weeks or months, unaccompanied by other symptoms except pruritus. This sequence developed in our cases also, 1 case showing jaundice for one hundred days and the other for twenty-six days. More recently Turner and his associates [13] in a report of their experience with 4,083 cases of acute hepatitis following yellow fever vaccination noted two types of hepatic reaction: one consisted of the usual hepatitis and was of brief duration; the other showed biliary obstruction of prolonged duration.

Thus it is clear that both drugs and infectious agents may produce a clinical and pathologic picture of obstructive jaundice as well as the more common hepatitis. Moreover, it is probable that a late stage of this hepatic injury may be the "intrahepatic cholangitic biliary cirrhosis" recently discussed by Karsner.[14] This end picture is especially characterized by cellular infiltration about the portal spaces and bile plugs in the biliary capillaries and canaliculi.

Granulocytopenia.—In the present series this complication occurred twice, with one fatality. Moderate granulocytopenia occurs with some frequency in thyrotoxicosis, expressing itself through a relative lymphocytosis. This, however, is probably not contributory to thiouracil granulocytopenia, since 1 of our patients had arteriosclerotic heart disease without thyrotoxicosis.

Astwood [6] noted this complication once in a series of 30 thyrotoxic patients treated with thiouracil and attributed it to excessive dosage. Williams and Clute [15] observed granulocytopenia at least twice in their series of 72 cases and noted other instances of leukopenia and granulocytopenia, which they ascribed to thyrotoxicosis as such. Gabrilove and Kert [7] noted 1 case of leukopenia in their series of 9 cases, but this case exhibited no percentile decrease in granulocytes.

The occurrence of granulocytopenia and agranulocytosis seems unrelated to the dosage level of thiouracil, since it has occurred in patients receiving as little as 0.2 Gm. daily or as much as 2.0 Gm. daily. The duration of therapy seems also not to be significant, as it has occurred from a few days [15] to many weeks following the inception of treatment. Intermittence of treatment is also not a factor, since it has occurred during uninterrupted therapy and has resulted fatally following remittent treatment. In addition, Williams and Clute [15] observed occurrence and disappearance of granulocytopenia during continued administration of thiouracil.

This toxic manifestation of thiouracil is therefore not predictable and certainly not always controllable, as evidenced by our 1 fatal case. In this patient correlative studies of the circulating blood, bone marrow sections and bone marrow smears [16] were carried out. These elucidate somewhat the mechanism of hemopoietic injury and recovery.

On April 1, 1943, when the thyrotoxicosis was first diagnosed and before any treatment had been given, the patient's hemoglobin was 95 per cent (13.8 Gm.), the red blood cells numbered 4,730,000 per cubic millimeter and the white blood cells numbered 5,600 per cubic millimeter, with 49 per cent neutrophils, 48 per cent lymphocytes, 11 per cent monocytes and 3 per cent eosinophils. Thus she exhibited the characteristic lymphocytic increase of thyrotoxicosis. As thiouracil controlled the thyrotoxicosis there was an increase in the leukocyte count to an average level of 8,000 per cubic millimeter. This normal level was maintained until her final admission to the hospital on April 17, when the leukocytes numbered 1,000 per cubic millimeter, with complete absence of granulocytes. On April 18 the leukocytes numbered 1,300 per cubic milli-

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16. Dr. Benjamin Alexander of the Hematology Clinic and Laboratory made the bone marrow studies.

meter, without any granulocytes. On this day a smear of the sternal marrow showed an appreciable reduction in the granulocytic series of cells with a conspicuous shift to the left. The few granulocytes present were chiefly in the myeloblast stage with exceedingly rare myelocytes. There was increased fragility of the white cells, as shown by large numbers of disintegrating cells with poorly staining nuclear material and vacuolated cytoplasm. All other elements in the bone marrow appeared normal.

On April 19 the leukocytes numbered 950 per cubic millimeter and the sternal marrow smear was unchanged. The bone marrow section showed increased fatty marrow and decreased red marrow. The predominating cells were normoblasts and erythroblasts. Only a rare granulocytic myelocyte was seen.

On April 21 the leukocytes numbered 1,150 per cubic millimeter, without granulocytes. At this time the sternal marrow smear showed an increased number of nucleated granulocytic cells with more promyelocytes and occasional myelocytes. The more mature forms of granulocytes were still greatly reduced. The bone marrow section showed a relative increase in fat cells and a noticeable absence of granulocytes.

On April 22, about twelve hours before death, the leukocytes numbered 1,650 per cubic millimeter, with 4 per cent myelocytes. A sternal marrow smear obtained post mortem showed an improving picture with more myelocytes, occasional metamyelocytes and even some young neutrophils.

The toxic effect of thiouracil on the bone marrow appears to be characterized by disappearance of mature granulocytes. This disappearance may be due to two factors: a disturbance in maturation at the promyelocyte stage or direct destruction of cells beyond the promyelocyte stage by the drug. As evidence of this destruction, one may note the large numbers of disintegrating forms seen in the bone marrow smears. It is, of course, also possible that similar destruction of granulocytes may have occurred in the peripheral blood, adding to the rapidity of onset of the agranulocytosis. Destruction of leukocytes in the blood stream as a possible mechanism of leukopenia has been discussed by Lawrence.[17]

The course followed by this patient was similar to that described by Plum [18] as generally true of all cases of agranulocytosis. He postulated three stages of the disease as regards the bone marrow: one with a bone marrow depleted in cells, another with a cell rich marrow characterized by early regeneration without mature myeloid forms and a third stage with a normal marrow picture found in patients dying of complications in spite of hematologic recovery. Our patient died of tracheal obstruction as she was entering Plum's third stage of marrow recovery.

Drug Fever.—In the present series 2 cases of typical drug fever reactions occurred on the ninth and eighteenth days respectively. Astwood [6] observed 2 instances of this complication in the first 30 cases of hyperthyroidism treated with thiouracil. Gabrilove and Kert [7] observed 2 instances of drug fever in their series of 9 cases of toxic goiter. Williams and Clute [15] refer to only 1 instance of drug fever in their series of 72 patients.

The mechanism of drug fever caused by thiouracil is as obscure as that caused by the sulfonamides. Some type of drug allergy must be predicated because readministration of the drug caused reappearance of the fever. As has been noted with other sensitizing drugs, such as arsphenamine or the sulfonamides,[19] dermatitis and lymphadenopathy may occur as additional signs of sensitization. In our series 1 patient had an urticarial dermatitis prior to the onset of granulocytopenia but associated with fever (case 2), while a second patient had splenomegaly (case 6). As with the sulfonamides, fever may be the precursor of more serious toxic reactions.

Swelling of the Submaxillary Salivary Glands.—Swelling of the submaxillary salivary glands was noted in 2 cases in the present series. While the reaction was fairly severe in 1 case, thiouracil was continued and the swelling subsided. Williams and Clute [15] report similarly. Obviously this manifestation is not a serious one and by itself no contraindication to thiouracil treatment.

As one reviews the toxic manifestations of thiouracil a noteworthy analogy to the sulfonamides emerges. The sulfonamides possess some antithyroidal and goitrogenic properties but to a lesser extent than thiourea derivatives. In the development of granulocytopenia and agranulocytosis, dermatitis, drug fever, jaundice and probably anemia, there is much parallelism. Both are sensitizing drugs, and this is the likely explanation of their similar toxic effects, since they are quite unrelated in chemical structure.

Thiouracil is a potent agent in the treatment of thyrotoxicosis, but it has dangerous toxic effects which so far have proved unavoidable and unpredictable, thus seriously limiting the use of the drug. Goldsmith and his co-workers [20] have suggested the addition of liver or folic acid to prevent thiourea-induced granulocytopenia on the basis of satisfactory protection in rats. The high percentage of rats which developed granulocytopenia and anemia following thiourea is striking. The validity of their suggestion in man, as well as its applicability to thiouracil, remains to be demonstrated and is at least open to the criticism that the normal percentage of neutrophils and lymphocytes in the rat's blood is exactly the inverse of that normally found in man.

SUMMARY AND CONCLUSIONS

1. Thiouracil was administered to 43 patients with toxic goiter and to 1 patient with hypertensive and coronary heart disease without thyrotoxicosis. Eight of these patients developed toxic reactions, as follows: 1 fatal case of agranulocytosis and 1 nonfatal case of granulocytopenia, 2 cases of jaundice, 2 cases of drug fever and 2 cases of submaxillary salivary gland swelling.

2. Thiouracil is an effective drug for the treatment of thyrotoxicosis.

3. It is also an unpredictably toxic drug which may produce serious and uncontrollable effects, especially on the bone marrow and liver.

4. Its use should be carefully controlled until there are satisfactory methods of preventing or controlling its toxic properties.

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USE OF ALUMINUM HYDROXIDE AND OTHER NONABSORBABLE ANTACIDS

IN TREATMENT OF PEPTIC ULCER

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During the past eight years at the Cleveland Clinic aluminum hydroxide gel has been the principal substitute for absorbable alkalis in the antacid therapy of peptic ulcer. It has been included in the treatment of more than 3,000 patients. A report on this subject was given before this association four years ago.[1] My purpose in this communication is to show a trend in management, to report the experience of our group to date and to reemphasize a method of treatment which continues to give satisfactory results.

Obviously, each patient presents an individual problem. All clinicians are agreed that first attention should be given to the patient's general health, including his hygienic needs, such as living habits, physical and mental rest and proper nutrition. Since the cause of peptic ulcer is unknown, additional measures have been used in its treatment. The work of B. W. Sippy, published in 1915,[2] is familiar to all clinicians. Extensive experimental work since that time, summarized by Palmer,[3] has confirmed the value of antacid therapy.

Approximately eight years ago we saw a number of patients with peptic ulcer having renal calculi or other renal complications, and aluminum hydroxide gel was substituted for the usual Sippy powders. These patients made satisfactory progress, even though the number of interval feedings and doses of antacid per day were reduced. Since that time aluminum hydroxide gel or other nonabsorbable antacids have been used routinely, and the results of therapy have seemed as satisfactory as those obtained formerly with a more rigid plan of treatment.

Evaluation of any therapy in a disease of unknown cause which is subject to spontaneous remissions is, of course, difficult. Jordan[4] has said that "the statistics which concern living patients with ulcer are never final, since in this disease, so characterized by recurrences, the cures of today may be nullified tomorrow. The life history of ulcer can be said to end only with the life of the patient." Palmer has pointed out that the results depend on the location and size of the lesion as well as the complications present, on the patient's willingness and ability to cooperate and on the physician's knowledge, enthusiasm and painstaking care in the management of the case at hand.

During the past eight years the incidence of peptic ulcer based on total registration each year has increased 100 per cent.[5] Nevertheless the percentage of patients having operations for duodenal ulcer during the same period has not notably increased, as shown in the chart. Although it is realized that this curve deals with a consultation practice, that a certain percentage of patients have operations elsewhere, that indications for surgery change from time to time and that more patients with surgical problems may be seen in some years than in others, it shows a trend in the management of this problem.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

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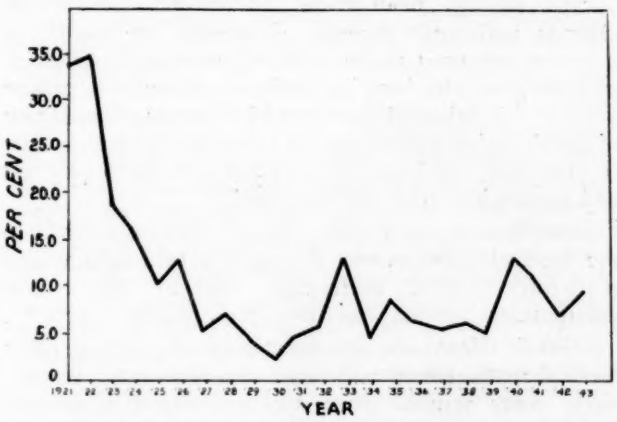
5. Mrs. Morgan of the clinic records department compiled these figures.

PRESENT PROCEDURES IN MEDICAL MANAGEMENT

The intensity of therapy naturally varies with the severity of the disease and must be individualized. Although hospital observation at the beginning of treatment has many advantages, in these wartimes most of our patients with peptic ulcer continue with their work during treatment.

Diet.—Except for patients having pyloric obstruction, the diet has been liberalized in recent years. The gain in weight in undernourished persons has been gratifying. During the first week a bland diet is used. For patients having massive hemorrhage, ground meat is used at the beginning of treatment. Otherwise meat,



Percentage of cases of duodenal ulcer treated surgically.

cooked vegetables and fruit are added during the second week, and within one month the patient has a well balanced diet except for the avoidance of seeds, skins and coarse fibers. Supplemental vitamin therapy is adjusted to the nutritional requirements of the individual.

Interval Feedings.—A glassful of milk and cream, malted milk tablets or other foods selected from the diet list are used at least once between meals, and the patient is advised to continue interval feedings the rest of his life.

During the first month's treatment most of our patients have interval feedings every second hour during waking hours. The patient is advised to resume two hour feedings each year at the times of seasonal recurrences, upper respiratory infections and emotional disturbances, even though there is a continued absence of symptoms.

Aluminum Hydroxide Gel.—Method 1. This antacid is usually given every two hours during waking hours in the first month's treatment and on alternate hours with the feedings, so that every hour the patient takes either food or antacid. The size of the dose depends on determinations of gastric acidity and the severity of the symptoms but is never less than 2 drachms

(8 cc.), and the bedtime dose is never less than 1 ounce (30 cc.). If the patient has severe night pain associated with continuous night secretion, the bedtime dose is repeated at midnight and at 3 a. m. during the first week's treatment.

In certain cases the continuous intragastric drip, first advocated by Winkelstein [6] and modified by Woldman and Rowland,[7] is used in administering aluminum hydroxide gel during the first one or two weeks' treatment.

Method 2. On the other hand, patients having uncomplicated ulcer with minor symptoms may continue working and may take the antacid only six times daily from the start of management, i. e. one hour after meals, one hour after the interval feedings and at bedtime.

Constipation is prevented by adding equal parts of heavy magnesium oxide and calcium carbonate to the evening doses of aluminum hydroxide gel. This enhances the antacid effect, and usually 1 drachm taken two or three times during the evening hours proves adequate. The amount is reduced as the residue in the diet is increased. For patients having temporary pyloric obstruction fluidextract of cascara sagrada and small enemas, if needed, are used. If narcotics are used at the start of treatment, particular care is given to bowel function. When the patient is on a well balanced diet he seldom needs the addition of any laxative substance. If constipation is unusually troublesome, combinations of aluminum hydroxide gel and magnesium trisilicate are used.

Complications of Peptic Ulcer.—Our experience in the medical management of massive hemorrhage and temporary pyloric obstruction due to spasm and inflammatory edema has been reported elsewhere.[8]

Jejunal Ulcer.—In the treatment of jejunal ulcer medical management undergoes a severe test. In previous years jejunal ulcer was considered a surgical problem as soon as the diagnosis was established. Although surgical procedures were used for patients having subacute perforation with abscess formation and gastrojejunocolic fistulas, 18 patients made satisfactory progress while using medical management.[9] These patients were observed and had follow-up studies during the years 1930 to 1941.

Based on the work of Ivy and his co-workers [10] in 1941, we now commonly use aluminum phosphate gel subsequent to any surgical procedure for peptic ulcer for a period of two or three months, particularly for patients who have had recurrent jejunal ulcer. Aluminum phosphate gel is also used for patients with peptic ulcer who have diarrhea or evidence of pancreatic deficiency and have been placed on a low phosphorus diet. However, most patients with peptic ulcer use a diet containing adequate phosphorus and have normal bowel function. Therefore, in most cases aluminum hydroxide gel is used, particularly in view of the fact that it has higher antacid properties.

6. Winkelstein, A.: A New Therapy of Peptic Ulcer: Continuous Alkalinized Milk Drip into the Stomach, Am. J. M. Sc. **185**: 695-703 (May) 1933.

7. Woldman, E. E., and Rowland, V. C.: New Technic for the Continuous Control of Acidity in Peptic Ulcer by the Aluminum Hydroxide Drip, Am. J. Digest. Dis. & Nutrition **2**: 733 (Feb.) 1936.

8. Collins, E. N., and Knowlton, R. S.: Review of One Hundred and Forty-One Consecutive Cases of Massive Hemorrhage from the Upper Gastrointestinal Tract, Ohio State M. J. **35**: 1175 (Nov.) 1939. Collins, E. N., and Rossmiller, H. R.: Obstructive Symptoms Versus Pyloric Obstruction: The Importance of Medical Management, S. Clin. North America **21**: 1495 (Oct.) 1941.

9. Collins, E. N., and Ward, G. J.: Current Trends in the Treatment of Jejunal Ulcer, Cleveland Clin. Quart. **9**: 159 (Oct.) 1942.

10. Fauley, G. B.; Freeman, Smith; Ivy, A. C.; Atkinson, A. J., and Wigodsky, H. S.: Aluminum Phosphate in Therapy of Peptic Ulcer: Effect of Aluminum Hydroxide on Phosphate Absorption, Arch. Int. Med. **67**: 563 (March) 1941.

CHECK-UP EXAMINATIONS

The aim in treatment is, of course, more than the immediate relief of symptoms. In order to have assurance that response to medical treatment is satisfactory, ulcer craters must disappear by progress roentgen examinations and also by gastroscopy for patients having gastric or anastomotic ulcers. These progress examinations are timed according to the severity of the initial problem. If they are unfavorable, the patient's condition is considered to be a surgical problem. If they are favorable, medical management is continued, but the patient is advised to have further check-up examinations during the first year's treatment and at least once a year during the next several years.

FOLLOW-UP THERAPY

If the patient continues medical management, he is advised to use method 2 as outlined, during the second and third months. During the remainder of the first year he is advised to use method 3, which includes one interval feeding between meals and the use of aluminum hydroxide gel or some other nonabsorbable antacid four times daily, i. e. one hour after meals and at bedtime. Furthermore, he is advised to resume method 3 each year at the times of seasonal recurrences, upper respiratory infections or emotional disturbances for at least five years, even though there is a continued absence of symptoms.

In recent years many forms of nonabsorbable antacids have become available. In our experience liquid alumina gel preparations, their combination with magnesium trisilicate, and the liquid form of magnesium trisilicate are more effective antacids than powder, tablet or capsule preparations. After the first month the patient continues to use the liquid preparations at least while at home. If convenience while working in a factory is important and his condition continues to be satisfactory, adequate dosage of one of the other preparations is permitted during working hours.

COMMENT

The treatment described does not completely neutralize gastric acidity. Originally, hourly gastric aspirations were made on hospital patients over twenty-four hour periods, and the dosage of antacid adjusted accordingly. The aim was to keep the level of free acidity low enough to prevent activation of pepsinogen, the proteolytic neutralization point emphasized by Hollander.[11] However, Eyerly and Breuhaus,[12] in measuring acidity and protein digestion within the human stomach, were unable to detect any eggwhite digestion in the stomach when its contents were maintained at a p_H of 3.5 or higher over a three hour test period. The Komarovs [13] and Schiffrin and Komarov [14] demonstrated the pre-

11. Hollander, F.: What Constitutes Effective Neutralization of Gastric Contents? Am. J. Digest. Dis. **6**: 127 (April) 1939.

12. Eyerly, J. B., and Breuhaus, H. C.: A Method of Measuring Acidity and Protein Digestion Within the Human Stomach, Am. J. Digest. Dis. **6**: 187 (May) 1939. Breuhaus, H. C., and Eyerly, J. B.: Antacids: Their Effect by Titration and Within the Human Stomach, Ann. Int. Med. **14**: 2285 (June) 1941.

13. Komarov, S. A., and Komarov, Olga: The Precipitability of Pepsin by Colloidal Aluminum Hydroxide, Am. J. Digest. Dis. **7**: 166 (April) 1940.

14. Schiffrin, J. J., and Komarov, S. A.: The Inactivation of Pepsin by Compounds of Aluminum and Magnesium, Am. J. Digest. Dis. **8**: 215 (June) 1941.

cipitation and inactivation of pepsin in vitro and in vivo in dogs by the alumina gels without excessive reduction of acidity.

James Flexner and his associates,[15] using a method for the continuous recording of gastric p_H in situ, which included a pumping system to maintain circulation of the mixture around the glass electrode, studied the efficacy of numerous antacids and found that aluminum hydroxide gel had a prolonged antacid effect when given in suitable dosage. Therefore fewer but larger doses are used each day than formerly, which is more convenient for the patient.

Aside from their acid combining power and the power of inactivating pepsin, the alumina gels have advantages over the usual alkalis. Their astringent and demulcent properties are of value and, unlike sodium bicarbonate, they do not cause a compensatory stimulation of acid secretion. They are not absorbed and therefore can be given without the hazards of alkalosis. In none of our cases was there a disturbance of the acid-base balance or urinary complications.

SUMMARY

1. A plan of medical management of peptic ulcer at the Cleveland Clinic has proved satisfactory in 3,000 cases during the past eight years.

2. Nonabsorbable antacids, principally aluminum hydroxide gel, have been included in this treatment. Aluminum phosphate gel has had increasing use, particularly in patients on a low phosphorus diet who have pancreatic deficiency or give a history of recurrent jejunal ulcer.

3. During the same period the incidence of peptic ulcer has increased 100 per cent, while the percentage of patients having operations for duodenal ulcer has not notably increased.

4. Supervised management over the lifetime of the patient should be adopted.

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ABSTRACT OF DISCUSSION

DR. JAMES FLEXNER, New York: Duodenal ulcer occurs in susceptible persons who become conditioned to their environment in such a way that there is an excessive outpouring of vagal substance (acetylcholine), which causes hypermotility, hypersecretion and altered circulation. This represents trauma, which, when uninterrupted, results in ulcer formation. The approach to the problem, therefore, may be divided into three phases: (1) environment, (2) the patient's response to the environment and (3) the resulting abnormal physiology. The environment may be temporarily altered by hospitalization or bed rest, but permanent alteration of the environment is often not practical. For the second phase of the problem, the patient may be given mild sedation and insight into his difficulties, but again lasting changes, even with psychoanalysis, are not practical and never too successful; therefore the remaining and most practical therapeutic approach is to attempt to correct the abnormal physiology. This entails interruption of the cycle of hypersecretion, irritability and spasm, which perpetuate the ailment and cause the patient's symptoms. I agree with Dr. Collins in the liberalization of the diet, as it is important that the diet be balanced. Antispasmodics are helpful, but our chief weapon, as Dr. Collins indicates, is buffer therapy. The most useful of all buffers are those which have a prolonged effect but which tend to keep the range in p_H between 7 and 3.5, though the efficacy probably persists to a p_H of 2.5. Both in practical experience and in experimental studies I have found colloidal aluminum hydroxide with half portions of magnesia magma in a glass of water to be the most satisfactory therapeutic agent. The average dose employed is aluminum hydroxide ½ ounce and milk of magnesia 1 drachm after meals, and, when necessary, a double dose at the hour of sleep. It is imperative, however, that each case be adequately buffered even if it is necessary to employ three or four times the dosage stated. In obstructive cases, after careful lavage, large doses of this mixture are administered for twenty-four to forty-eight hours, with parenteral feedings, and for weeks or months in addition the patient should receive postprandial buffer mixture and the stomach should be emptied at night with a large tube, followed by a double dose of the medication. With this procedure remarkable medical rehabilitation is possible in obstructive cases.

DR. WALTER L. PALMER, Chicago: I too have enjoyed this paper and I also enjoyed Dr. Flexner's discussion of it. I should like to ask Dr. Collins and also Dr. Flexner why they consider aluminum hydroxide to be superior to that very cheap and universally available preparation calcium carbonate?

DR. EVERETT N. COLLINS, Cleveland: We started using aluminum hydroxide gel in peptic ulcer patients having renal calculi or other renal complications because our urologists insisted on an acid urine and no disturbance in the acid base balance. They said "Do not give chalk to these patients because they will have a strongly alkaline urine and in the absence of adequate vitamin therapy they may develop more stones." We found that we could maintain an acid urine with aluminum hydroxide gel because it was not absorbed. A second reason for our using this preparation in preference to our former use of calcium carbonate was that hourly gastric aspirations during twenty-four hour periods of treatment demonstrated that the antacid effect was maintained over a longer period of time than with calcium carbonate. Fewer but larger doses of aluminum hydroxide gel had a prolonged effect which was not obtained with calcium carbonate. Since then treatment has been simplified for the patient, as compared with strict Sippy management. As mentioned in the text, we add a laxative powder consisting of calcium carbonate and heavy magnesium oxide as needed to prevent constipation at the start of treatment. When the patient is on a well balanced diet its use is seldom necessary.

15. Flexner, J.; Kniazuk, M., and Nyboer, J.: Method for Continuous Recording of Gastric p_H in Situ, Science **90**: 239 (Sept. 8) 1939. Flexner, J., and Kniazuk, M.: A Method for the Continuous Recording of Gastric p_H in Situ: II. Experimental Details, Am. J. Digest. Dis. **7**: 138 (March) 1940; A Method for the Continuous Recording of Gastric p_H in Situ: III. Evaluation of the Efficacy of Certain Antacids, ibid. **8**: 45 (Feb.) 1941. Rossett, N. E., and Flexner, J.: A Method for the Continuous Recording of Gastric p_H in Situ: IV. Further Evaluation of the Efficacy of Antacids in Vitro and in the Human Being, Ann. Int. Med. **18**: 193 (Feb.) 1943.

Sigmund Freud.—In paying tribute to the memory of Sigmund Freud, the task of the neurologist differs in some measure from that of the psychoanalyst in that the former is more organically minded and possibly more objective scientifically. To say that Freud was a great man or that he made important contributions is somewhat of a platitude, which from the mouths of certain critics represents only an ill concealed hostility. It is doubtful whether the time has yet arrived to permit objective criticism; and yet a certain degree of detachment is not altogether impossible. Like all great men, perhaps more than most Freud has been both reviled and misunderstood in his own day. Many of his opponents did not actually read all his works, and those who did approached them with a bias which made sympathetic understanding extremely difficult. Others, who merely did lip service to psychoanalysis, did Freud great injustice with their ambivalent praise. Many critics and some outright opponents appropriated much of what he contributed, then proceeded to belabor him with his own weapons. But even greater injustice was done to Freud by those of his followers who swallowed uncritically much that was scientifically indigestible. Many of the hypotheses and theories of Freud are not at all solid, and to accept all of them and defend them foolishly as facts is to do violence not only to the greatness of the man but to much which promises to be of enduring worth. Some of Freud's followers seemed to thrive on borrowed wisdom and donned a cloak of omniscience which did not altogether conceal the barren spaces beneath it. Since all argumentum ad hominem is generally fallacious and frequently evasive, it is obviously unfair to judge Freud's contributions either by his opponents or by his followers.—Wechsler, I. S.: The Neurologist's Point of View, New York, L. B. Fischer, 1945.

PHYSICAL IMPAIRMENT AND JOB PERFORMANCE

A COMPARATIVE STUDY OF ACCIDENT EXPERIENCE, PRODUCTION AND EFFICIENCY, SICK ABSENTEEISM AND TURNOVER AMONG 2,858 PHYSICALLY IMPAIRED AND 5,523 ABLE BODIED WORKERS IN GOVERNMENT INDUSTRY

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A comparative study of 2,858 physically impaired workers and 5,523 able bodied workers employed in forty-three establishments of the War and Navy Departments, situated in various parts of the country, has been conducted by the Medical Division of the United States Civil Service Commission. It has yielded information which will be of assistance to the commission in carrying out its responsibilities for placement of disabled veterans and will contribute to the solution of problems affecting many thousands of physically impaired civilians and war veterans seeking employment in the federal service.

Men and women in the armed forces are being injured in a maiming war. Advancements in medical science are saving lives, but the number and severity of the injuries being sustained by members of the armed forces are such that this nation will be faced with the greatest problem of rehabilitation in its history. Rehabilitation is not complete unless it results in employment of feasible cases through judicious placement.

Many disabled veterans of the last war were employed without regard to their highest skills or to their physical and mental capacities or to the satisfaction of the employer. Lack of consideration given to these factors in placement caused dissatisfaction on the part of the employer, the employee and organizations interested in the welfare of veterans. The aftermath was the stigmatizing of the disabled veteran because of his disability; the truly pertinent factors, such as the veteran's skills and capacities, became secondary considerations.

The placement of the disabled veteran in a suitable position involves proper consideration of his mental, vocational and physical capacities as they relate to the requirements of the job. In this connection there still will be a need for educating personnel officials on the employment of the physically impaired, and it can be expected that difficulty of the impaired in securing employment may be again accentuated when present wartime labor shortages are relieved.

Policies leading to the employment of the physically impaired should not be merely emergency measures; rather, the objective of these policies should be to bring forward a contribution to the solution of the overall problem which will be of even greater significance after the war. Notions concerning job performance of the impaired based on theory or opinion must give way to those based on factual information. The former have been used in the past as a guide by many personnel officials and their medical and safety advisers in recommendations for the employment or nonemployment, of physically impaired individuals. This contributed to the development, on the part of labor groups, of an antagonistic attitude toward the idea of preemployment examinations, and some of these groups have gone so far as to forbid their members to submit to such examinations.[1] Equal antagonism of veteran organizations can be expected in the postwar era if unjustifiable restrictive employment policies relating to the physically impaired persist, either in federal or in private employment.

Never before has the commission been presented with a more favorable opportunity to develop data on job performance of the physically impaired. Studies[2] of the physical demands of jobs in the federal service, together with wartime demands for workers in all types of trades and crafts, have caused a lowering of physical standards for employment and have brought about a nationwide program for the judicious placement of impaired workers in the federal service. More than 44,000 persons with severe physical defects (table 1) were placed in government industrial establishments between October 1942 and December 1944. The majority of these persons were placed according to (1) their educational, training and experience qualifications and (2) their physical capacities, which were matched with the physical demands of the job as determined by job analysis.

Several studies of job performance of the physically impaired have been conducted in private industry. The Western Electric Company's study demonstrated that among 652 impaired workers there were fewer absences because of illness and a lower accident rate than among employees with all their physical faculties; production records of the impaired were found to be satisfactory, and in individual cases the impaired displayed superior ability.[3]

In 1943 the U. S. Office of Education invited a number of employers of rehabilitated workers in private industry to report on the general efficiency of this group as compared with that of able bodied workers. The employers were asked to compare their impaired workers with the able bodied workers on the basis of (1) rate of production, (2) rate of absenteeism, (3) rate of turnover and (4) frequency rate of accidents. Replies were received from more than 100 employers, most of whom are executives of large corporations engaged in the manufacture of war materials and equipment; most of them employ a considerable number of persons with physical impairments. These replies indicated conclusively that the physically impaired workers produced as much as, or possibly a little more than, the able bodied workers. A more significant fact, however, was that they were practically unanimous in reporting that the physically impaired are dependable, regular in attendance and careful in observance of safety regulations.[4]

On the basis of a canvass by mail of employers of impaired workers in industry, the Division of Industrial Hazards, Bureau of Labor Statistics, U. S. Department

1. Zimmer, V. A.: Employment Handicaps of the Physically Disabled Worker, in Proceedings of the National Conference on Employment of the Disabled, Washington, D. C., Nov. 21-23, 1941.
2. Harvey, V. K., and Luongo, E. P.: The Physically Handicapped in Industrial Establishments of the Government: Possibilities for Their Increased Placement, J. A. M. A. **121**: 100 (Jan. 9) 1943. Operations Manual for Placement of the Physically Handicapped, ed. 3, June 1944, U. S. Government Printing Office, Washington 25, D. C.
3. Dietz, J. W.: An Experiment with Vocationally Handicapped Workers, Western Electric Company, 1931.
4. The Production Efficiency of Physically Impaired Workers, Federal Security Agency, United States Office of Education, Washington, D. C., 1943.

of Labor, reported that these workers are just as efficient in the jobs they hold as their unimpaired fellow workers. With regard to absenteeism, injury frequency rate and labor turnover, the physically impaired were rated as superior to the unimpaired.[5]

The Minneapolis Artificial Limb Company's study of 145 employees, 95 per cent of whom were disabled, showed work absences caused directly or indirectly by physical disability to be practically unknown, and labor turnover was negligible.[6]

An excellent productivity and attendance record was demonstrated among impaired workers in Brooklyn's Sheltered Industries and in the Illinois Industry for the Blind, which employed groups of physically impaired men and women, more than half of whom were blind. These workers were awarded the Maritime Commission's M for excellence in workmanship; a factor in the award was the noteworthy attendance record (98.5) achieved by the group during the winter months.[7]

More recently Poole and Bent,[8] Lockheed Aircraft Corporation, undertook an extensive study of workers in the cardiac group and demonstrated that, when impaired workers with cardiac lesions were judiciously placed in industry, compensation, production and personnel costs generally are not increased as a result of the disability.

METHOD

Within the limitations placed on the Civil Service Commission by time, statistical material available and personnel which could be assigned to the project, the study in War and Navy Department establishments was conducted with the greatest possible objectivity. In this sample study the first step was to obtain a list of impaired workers in each establishment or plant. This was accomplished before going to the plant by reviewing placement reports of the physically impaired which the commission receives from appointing officers on a semimonthly basis and, to bring the list up to date, by securing additional names from state and local rehabilitation agencies and from the plant itself.

In selecting impaired workers for the study, only serious physical defects were considered. Stress was laid on those physical defects most likely to be encountered in the placing of disabled veterans—orthopedic defects (including amputations and deformities), visual and hearing defects and arrested tuberculosis.

In selecting able bodied workers to be matched with the physically impaired, the records of all such workers employed on the same jobs, and under the same supervisors, as the impaired were examined. For the purpose of control, from 1 to 3 of these able bodied workers were selected at random and matched with physically

TABLE 1.—*Placement Report of the Physically Impaired*

Current Report—November 1 to December 1, 1944

Civil Service Regions	Disabilities: Orthopedic Defects: Upper Extremities	Orthopedic Defects: Lower Extremities	Orthopedic Defects: Spinal Column	Blindness: One Eye	Blindness: Both Eyes	Hearing Defects: Hard of Hearing	Hearing Defects: Totally Deaf	Tuberculosis Arrested	Heart Disease Compensated	Dwarfism	Current Totals
1st	40	67	9	69	1	27	6	73	57	1	350
2d	40	78	11	20	1	17	4	3	16	0	190
3d	26	39	6	36	4	18	0	2	29	0	160
4th	34	57	15	22	0	11	3	1	11	0	154
5th	78	109	20	55	0	26	3	13	62	0	366
6th	40	51	22	56	21	28	0	9	39	0	266
7th	25	55	14	15	0	4	2	5	17	0	137
8th	16	23	9	13	1	9	0	3	10	0	84
9th	47	67	15	41	0	20	4	1	33	0	228
10th	12	18	2	12	1	2	0	0	4	0	51
11th	31	51	15	15	2	8	1	2	18	0	143
12th	26	43	14	23	2	6	3	0	2	0	119
13th	24	36	6	9	2	12	0	4	12	0	105
Current totals	439	694	158	386	35	188	26	116	310	1	2,353
Previously reported	9,728	13,641	2,083	8,091	590	3,423	1,091	1,489	4,023	185	44,344
Grand totals	10,167	14,335	2,241	8,477	625	3,611	1,117	1,605	4,333	186	46,697

Regions	Grand Totals: Disabilities * Previous	Current	Grand	Placements * Previous	Current	Grand	Physically Impaired Veteran Placements † Previous	Current	Grand
1st	6,436	350	6,786	6,321	332	6,653	1,235	118	1,353
2d	4,556	190	4,746	4,356	185	4,541	230	52	282
3d	3,340	160	3,500	2,972	153	3,125	194	35	229
4th	1,948	154	2,102	1,858	141	1,999	123	2	125
5th	6,391	366	6,757	6,119	361	6,480	698	123	821
6th	3,060	266	3,326	2,888	255	3,143	165	29	194
7th	2,175	137	2,312	2,020	127	2,147	199	37	236
8th	1,463	84	1,547	1,369	81	1,450	164	14	178
9th	3,932	228	4,160	3,641	227	3,868	406	48	454
10th	1,578	51	1,629	1,490	50	1,540	38	1	39
11th	2,569	143	2,712	2,408	141	2,549	237	33	270
12th	4,706	119	4,825	4,280	108	4,388	240	14	254
13th	2,190	105	2,295	2,101	102	2,203	144	16	160
Grand total	44,344	2,353	46,697	41,823	2,263	44,086	4,073	522	4,595

* Since Oct. 1, 1942. † Since July 1, 1943 and included in placement totals.

5. Impaired Workers in Industry, United States Department of Labor, Bureau of Labor Statistics, October 1944; Monthly Labor Rev., volume 59, no. 4.

6. Trautman, Ray: We Hire Men and Women Who Are Physically Handicapped, Factory Management and Maintenance, January 1943.

7. Marine Engineering and Shipping Review, New York, June 1943.

8. Poole, F. E., and Bent, J. R.: The Employment of Cardiacs, Indust. Med. **13**: 479 (June) 1944.

impaired workers according to (1) sex, (2) age (within ten years unless more than 50 years of age, in which case, within five years), (3) length of experience on the job and (4) salary. In the matching process two schedules were filled out for each worker and one schedule for each section [9] of the plant, from which samples were selected.

The sectional report was an overall control on the attendance, accident rate and turnover records of the section. It provided general information with regard to the kind of work performed in the section, job titles and physical activities required. It showed the total number of employees in the section at the time of the survey (also the yearly average) and the approximate number of disabled employees in the section, both at the time of the survey and by yearly average. Where an industrial medical service was available in the establishment, the report indicated whether it was full time or part time or consisted simply in providing for a physician on call. Sectional reports described procedures used in assuring that appropriate work assignments were given to physically impaired workers.

The individual schedules—two were used for each worker in the groups being compared (physically impaired and able bodied)—furnished information on

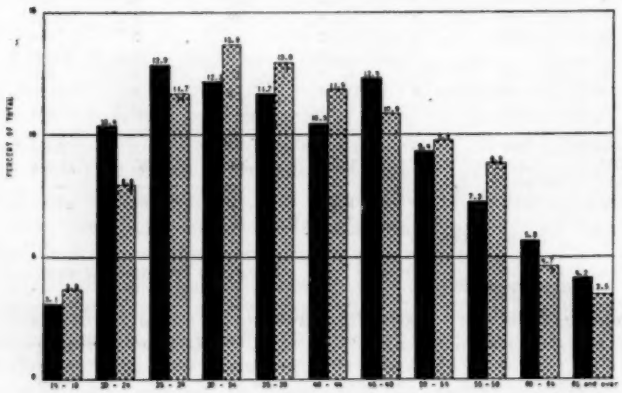

Chart 1.—Percentage distribution of physically impaired (black columns) and able bodied (stippled columns) workers by age groups.

(1) title of present position, (2) annual salary at beginning of employment and salary at time of survey, (3) period of employment on present job, (4) attendance records (days lost because of sickness, annual leave and other causes), (5) efficiency ratings, (6) accident records from the standpoint of lost time injuries,[10] the number of days lost because of injuries and, in the case of the physically impaired, the relationship of lost time injury to preexisting impairment, and (7) quantity and quality productivity (as compared with that of other workers).

In the case of the physically impaired, the schedules show in addition (1) the foreman's or supervisor's opinion on the relationship of the physical impairment to the performance of the work, (2) his comments with regard to job tailoring which may have been neccesary, and special considerations which may have been given to the worker, because of the worker's disability, and (3) a complete description of the worker's disability.

The use of individual schedules for each worker sampled eliminated consolidated general opinions of supervisors or foremen on the impaired as a group, or on the able bodied as a group, and made it possible to consider each individual worker from the standpoint of job performance.

Reports were obtained through cooperation of personnel officials, safety officers, safety engineers and medical officers. All establishments had safety officers, 80 per cent of the establishments reported full time medical supervision, and 20 per cent reported a part time medical officer or a physician on call. Supervisors and foremen, although given complete instructions with regard to filling out the reports, were not given information to the effect that the purpose of the study was to evaluate the job performance of physically impaired workers. The reports received as a result of the survey were processed and statistically evaluated centrally by the Medical Division and the Statistical Services Section of the Commission in Washington, D. C.

Out of approximately 3,300 physically impaired worker cases received, 442 were invalidated for various reasons, such as physical defects of a nature that raised a question as to whether these defects were handicaps, job experience variations not in accord with the control method of the study, insufficient information on various aspects of job performance, wide variations in age of matched workers, inclusion of both men and women in groups to be matched and contradictory reporting. When cases of physically impaired workers were invalidated, the cases of able bodied workers matched with them also were discarded.

TABLE 2.—*Percentage Distribution of Physically Impaired and Able Bodied Male and Female Workers by Age Groups*

Age Group, Years	Physically Impaired			Able Bodied		
	Total	Male	Female	Total	Male	Female
Total: Number	2,858	2,380	478	5,375	4,427	948
Per cent	100.0	100.0	100.0	100.0	100.0	100.0
14-19	3.1	2.6	5.5	3.8	2.7	9.0
20-24	10.4	8.9	17.8	8.0	5.1	21.4
25-29	12.9	11.8	17.8	11.7	11.3	13.3
30-34	12.3	12.7	10.5	13.8	14.5	10.6
35-39	11.7	12.1	9.6	13.0	13.9	8.7
40-44	10.5	10.7	9.6	11.9	12.3	9.7
45-49	12.4	13.2	8.6	10.9	11.2	9.7
50-54	9.4	9.7	8.0	9.8	10.3	7.5
55-59	7.3	7.6	5.5	8.9	9.4	6.5
60-64	5.8	6.0	5.0	4.7	5.2	2.7
65 years and over	4.2	4.7	2.1	3.5	4.1	0.9
Median age	39.9	40.9	34.9	39.9	41.0	32.9

TABLE 3.—*Percentage Distribution of Physically Impaired and Able Bodied Workers by Occupation*

Occupation	Physically Impaired			Able Bodied		
	Total	Male	Female	Total	Male	Female
Total: Number	2,858	2,380	478	5,375	4,427	948
Per cent	100.0	100.0	100.0	100.0	100.0	100.0
Administrative, professional and related occupations *	2.1	2.2	1.5	2.3	2.5	1.1
Clerical	21.3	14.7	54.0	20.0	12.9	52.9
Service	3.6	3.5	4.0	3.5	3.4	3.7
Craftsmen	28.2	32.3	7.9	29.5	34.0	8.9
Operatives	18.7	18.9	17.8	19.3	19.3	19.4
Laborers	26.1	28.4	14.8	25.4	27.9	14.0

* Includes semiprofessional, technical and scientific workers.

9. In many plants, sections are equivalent in number of workers to divisions or departments in private industry.

10. An injury causing death, permanent impairment or absence from work beyond the day or shift on which the injury occurred.

CHARACTERISTICS OF WORKERS SAMPLED AND STUDIED

Age.—Table 2 and chart 1 show the percentage distribution of physically impaired and able bodied workers by sex and age. A remarkable occurrence is to be noted in the median for impaired workers (39.9) and the median for the able bodied workers (39.9). The median for female workers shows a variation of only two years, which is not thought to be significant in the age group considered from the standpoint of job performance.

The question of age is a factor of utmost importance in a study of this kind, since age may affect statistics on job performance for reasons which are unrelated to the presence or absence of physical defects. Farmer [11] in 1932, and more recently Kossoris,[12] have demonstrated that older workers have a lower accident frequency rate than younger workers but have a greater severity rate (with a longer average healing period) and a greater death rate and lose more time as a result of accidents. Mann [13] has demonstrated that the highest rate of accidents exists in the younger age group and that there is a progressive decline in rate as age increases.

From the standpoint of productivity, beyond 50 years of age there may be expected a diminution of productivity in certain types of trades involving repetitive manual tasks.[14]

With regard to absences, short term absences can be expected to be greater in the younger age groups since such groups can be expected to have a larger number of whims, diversions and social activities which are important as the underlying causes of short term absences. Schwartz [15] has demonstrated the existence of this tendency among younger groups of workers. Actual valid sickness absenteeism can be expected to be higher with advancing age because of the appearance of those diseases the incidence of which rises with advancing age.

In view of the median ages both for the male and for the female workers surveyed, it is believed safe to assume that the percentage of error in the job performance statistics because of age variation in the sample is negligible.

Sex.—Tables 3 and 4 present the percentage distribution of physically impaired and able bodied workers by sex and occupation. From the standpoint of statistics on attendance, accident experience and turnover rates sex, like age, has a relationship to job performance outside of any consideration of the presence or absence of physical defects.

In general, the rate of absenteeism of females due to sickness, and of turnover due to "quits," can be expected normally to be higher.[16] With regard to accidents, aside from the fact that females, as a group, are placed in less hazardous occupations, they normally can be expected to have a lower accident rate since, as a group, they are more painstaking and fastidious in job performance and they fear the consequences of accidents and, therefore, do not "show off." Further, they are more adaptive to routine and monotonous work.[13]

In the commission's study, 2,380 physically impaired males were matched with 4,427 able bodied males, and 478 physically impaired females were matched with 948 able bodied females. With this ratio of matching by sex, it is believed that the percentage of error in the job performance statistics for reasons extrinsic to physical condition is negligible.

TABLE 4.—*Percentage Distribution of Physically Impaired Workers by Type of Disability and Occupation*

Type of Disability	Total	Occupation					
		Craftsmen	Operatives	Laborers	Service	Clerical	Others *
Total: Number	2,858						
Per cent	100.0	28.2	18.7	26.1	3.6	21.3	2.1
Amputation of:							
Arm or arms	4.9	0.5	0.6	1.8	0.4	1.5	0.1
Hand or hands	1.5	0.2	0.2	0.5	0.2	0.4	†
Fingers	4.9	1.4	1.4	1.4	0.1	0.5	0.1
Foot or feet	0.9	0.4	0.1	0.2	†	0.2	...
Leg or legs	7.0	2.8	1.1	1.8	0.2	0.9	0.2
Disability or deformity of:							
Hip or shoulder	3.4	1.0	0.8	0.5	0.1	1.0	†
Back	5.3	1.3	1.1	1.7	0.1	1.0	0.1
Upper extremities	8.8	1.9	1.7	2.3	0.6	2.3	†
Lower extremities	20.5	5.0	4.3	4.9	0.8	5.0	0.5
Vision	19.8	5.8	3.8	6.4	0.5	3.1	0.2
Hearing	8.4	2.7	1.3	1.9	0.1	2.0	0.4
Cardiac	8.2	2.5	1.1	1.9	0.4	2.1	0.2
Tuberculosis (pulmonary)	5.3	2.1	0.9	0.7	0.1	1.2	0.3
Dwarf	0.4	0.1	0.1	0.1	...	0.1	...
Diabetes	0.1	0.1	...	...	...	...	...
Epilepsy	0.1	0.1	...	†	...	†	...
Pulmonary disease other than tuberculosis	0.5	0.3	0.2	...	†	...	...

* Includes administrative, professional, semiprofessional, technical and scientific workers.
† Less than 0.05 per cent.

TABLE 5.—*Percentage Distribution of Physically Impaired and Able Bodied Workers by Industry*

Industry	Physically Impaired	Able Bodied
Total: Number	2,858	5,375
Per cent	100.0	100.0
Aircraft installations	43.8	40.8
Ordnance activities	27.9	26.4
Shipbuilding and ship repair	17.0	21.8
Other manufacturing	2.8	4.0
Procurement, inspection, storage, supply	1.3	1.2
Administrative office	4.4	3.7
Camps, forts, naval training stations	2.8	2.1

Industry.—The establishments coming under this study represented diversified types of government industries with variations in occupational hazard exposure, production and employee relations policies and working conditions from the standpoint both of physical activities and of environmental factors.

The distribution of sampled workers by industry was as follows (table 5):

1. Of the physically impaired 43.8 per cent and of the able bodied workers 40.8 per cent were engaged in air-

11. Farmer, Eric: The Causes of Accidents, New York, Sir Isaac Pitman & Sons, Ltd., 1932.
12. Kossoris, M. D.: Relation of Age to Industrial Injuries, Monthly Labor Review, United States Department of Labor, Bureau of Labor Statistics, October 1940.
13. Mann, James: Analysis of 1,009 Consecutive Accident Cases at One Ordnance Depot, Indust. Med. **13**: 368 (May) 1944.
14. Smith, K. R.: Age and Performance on a Repetitive Manual Task, J. Appl. Psychol. **22**: 295 (June 12) 1938.
15. Schwartz, Leon: Evaluation of a Sick Report System, Personnel Administration, Society for Personnel Administration, Washington, D. C., **6**, number 10, June 1944.
16. Gafafer, W. M.: Sickness Absenteeism Among Male and Female Industrial Workers During 1943, and Among Males During First and Second Quarters of 1944, with Note on Respiratory Epidemic of 1943-44, Pub. Health Rep. **59**: 1267 (Sept. 29) 1944. Labor Turnover in Manufacturing, Mining, Telephone and Telegraph Industries, U. S. Department of Labor, Bureau of Labor Statistics, August 1943.

craft industry, involving the manufacture, repair, storage and inspection of aircraft and aircraft parts.

2. Of the physically impaired 27.9 per cent and of the able bodied workers 26.4 per cent were engaged in ordnance activities, including the manufacture, assembling and storage of ammunition and explosives, including artillery ammunition, small arms ammunition, metal shell components, torpedoes and all types of firearms, including large guns and their mounts and carriages. These activities were centered in arsenals, ordnance works and depots, armories, ammunition depots and torpedo stations.

3. Of the physically impaired 17.0 per cent and of the able bodied workers 21.8 per cent were engaged

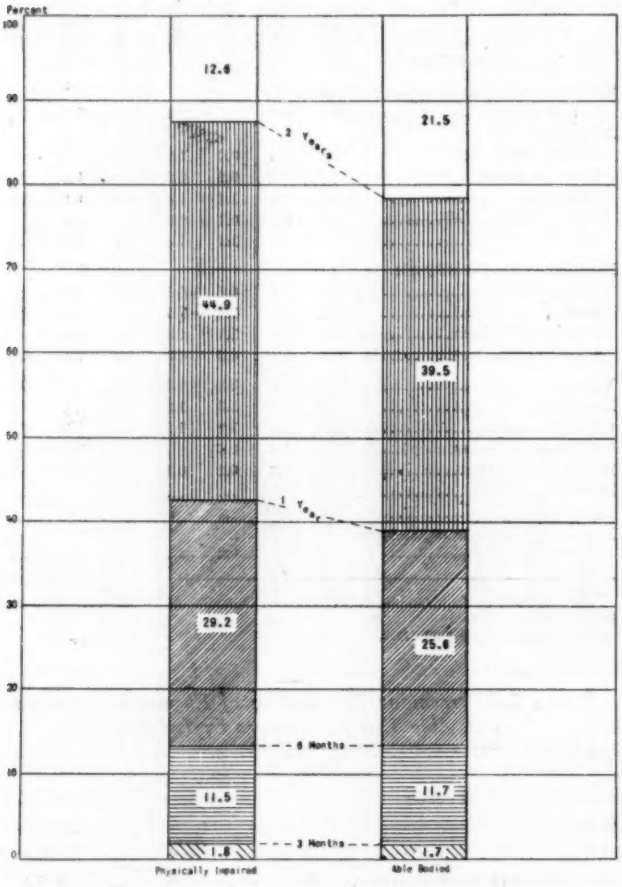

Chart 2.—Length of time in present job.

in shipbuilding and ship repair. These naval activities were centered in navy yards and naval drydocks.

4. Of the physically impaired 2.8 per cent and of the able bodied workers 4.0 per cent were engaged in manufacturing of types other than those mentioned. These workers were engaged in the manufacture and inspection of textiles, leather goods and clothing and were centered in quartermaster depots of the War Department and the clothing depot of the Navy Department, New York City.

5. Of the physically impaired 1.3 per cent and of the able bodied workers 1.2 per cent were engaged in procurement, inspection and supply. This activity excludes storage and supply for aircraft, ammunition, explosives, firearms and guns and also excludes manufacturing depots of the Army Quartermaster Corps and of the Navy. The army activities in this category included such facilities as army procurement and inspection districts or zones, purchasing offices and quartermaster depots, holding and reconsignment points and backup storage facilities. For the Navy, it included such facilities as matériel centers, supply depots and naval inspector offices.

6. Of the physically impaired 4.4 per cent and of the able bodied workers 3.7 per cent were employed in field administrative offices of the War and Navy departments, and a small number were employed in the Departmental Service, Veterans Administration, Washington, D. C.

7. Of the physically impaired 2.8 per cent and of the able bodied workers 2.1 per cent were in camps, forts and naval training stations; for the Army this includes such facilities as camps, forts, ordnance training centers, recruiting and induction districts, replacement depots and centers and reclassification centers; for the Navy it includes such facilities as naval training stations.

Occupation.—Tables 3 and 4 show the percentage distribution of workers by type of occupation. It is to be noted that the percentage distribution for the impaired and for the able bodied are approximately the same, with the heaviest distribution in both groups among craftsman, laborer, professional and service occupations.

The craftsman classification includes carpenters, cabinet makers, painters, machinists, millwrights, toolmakers, sheet metal workers, shipfitters, patternmakers, modelmakers, mechanics, repairmen, apprentices to skilled crafts and similar occupations.

The laborer group of occupations represents helpers and unskilled, semiskilled and skilled laborers; many of these occupations are closely related to those of craftsmen.

Included in the operative occupations are machine shop operatives, welders, flame cutters, sewing machine operators and related occupations, printing operatives, chauffeurs and drivers, learners and operators of motor vehicles.

The clerical group consists mainly of stenographers, typists, secretaries, telephone operators, statistical, technical and research clerks, accounting, fiscal and payroll clerks and purchasing and supply clerks.

The service workers are mainly janitors, charwomen, elevator operators, guards, watchmen and policemen.

The administrative, professional and related workers consist mainly of technical and scientific assistants, draftsmen, inspectors and procurement and supply officers.

Job Experience.—Table 6 and chart 2 present the percentage distribution of physically impaired and able bodied workers by length of time on the present job or job experience as demonstrated. The table shows comparable job experience for the two groups, with, however, a higher percentage of able bodied with experience on the job of two years or more. These figures are significant in evaluating the results of this survey, since it is axiomatic that experience on the job often determines how well, and in many instances how safely,[11] a job is performed.

Physical Defects Among Impaired Workers.—The presence or absence of physical defects among all workers who were sampled was determined on the

basis of a complete physical examination. Table 7 shows the percentage distribution of the physically impaired by sex and by type of disability. Of the male impaired workers 58 per cent and of the female impaired workers 53.6 per cent had orthopedic defects. Included among the orthopedic defects were deformities and amputations of arms, hands, fingers and feet and deformities of the back, hip and shoulder joints. In some cases studied there were multiple defects. Of the deformities, the majority were due to poliomyelitis; approximately 90 per cent of the amputations were due to accidents; the cause of disabilities of the back, hip and shoulder joints ranged from congenital deformities to chronic disease (arthritides and tuberculosis) and traumatic injuries.

As has been indicated, the commission wishes to study job performance of persons with physical defects which were likely to be found among a large number of disabled veterans. It is believed that the preponderance of orthopedic cases coming under this study accomplishes this objective.

Vision defects, including total blindness, industrial blindness and blindness in one eye, accounted for 20.2 per cent of the defects among physically impaired males and 17.4 per cent among physically impaired females. In studying the totally blind persons, cases were limited to those having not more than 20/200 visual acuity in the better eye, with correction, or visual acuity greater than 20/200 but with limitation of the field of vision such that the widest diameter of the visual field subtends an angle not greater than 20 degrees. The industrially blind group included persons with vision of not more than 20/100 in the better eye with optimum correction up to total blindness as described. Cases of blindness in one eye were limited to those with vision of 20/200 or less with best correction in the defective eye and with good vision in the other eye. No statistics were reported on causes of blindness in any of the visual defect groups described.

TABLE 6.—*Percentage Distribution of Physically Impaired and Able Bodied Workers by Length of Time in Present Job*

Length of Time on Job	Physically Impaired	Able Bodied
Total: Number	2,858	5,375
Per cent	100.0	100.0
Less than three months and unspecified	1.8	1.7
3 months, under 6 months	11.5	11.7
6 months, under 1 year	29.2	25.6
1 year, under 2 years	44.9	39.5
2 years or more	12.6	21.5

Hearing defects occurred at a rate of 7.6 per cent among physically impaired males and 12.4 per cent among females. The hearing defect group included both the deaf and the hard of hearing.

With regard to the deaf, cases were limited to those in which the residual hearing was nonfunctioning for ordinary purposes of life, the residual hearing in these cases being less than 1/20 in either ear. Practically all cases were without normal speech function; the cause was approximately evenly distributed between adventitious and congenital causes.

Cases of hard of hearing were limited to those in which there was some hearing but insufficient to carry on ordinary conversation at 10 feet or less without a hearing aid. This group included a large number of cases in the older age range in which the hearing defect was due to otosclerosis; however, in the great majority of these cases the hearing defects resulted from complications of childhood infectious diseases and to meningitis.

Heart disease was reported in 7.7 per cent of the physically impaired males and in 10.9 per cent of the females. Cardiac cases studied were limited to those with organic heart disease fully compensated; coronary and syphilitic heart disease were excluded. The majority of these cases were rheumatic in origin; a small number, however, were congenital in nature and some were due to hypertension.

TABLE 7.—*Percentage Distribution of Physically Impaired Workers by Sex and Type of Disability* *

Type of Physical Disability	Male	Female
Total: Number	2,380	478
Per cent	100.0	100.0
Amputation of:		
Arm	5.4	2.3
Hand	1.7	0.6
Fingers	5.2	3.2
Leg	7.4	2.9
Legs	0.5	...
Foot	1.0	0.2
Feet	†	...
Disability or deformity of:		
Hip or shoulder	2.8	4.2
Arm	5.9	5.0
Arms	0.6	0.2
Hand	1.6	2.3
Hands	0.2	0.8
Fingers	0.4	0.8
Leg	13.6	18.2
Legs	3.0	2.9
Foot	2.4	2.7
Feet	0.7	0.6
Back or spine	5.2	5.9
Hips or shoulders	0.4	0.9
Vision defects:		
Blind	1.7	3.6
Blind in one eye, sound vision in other	18.5	13.8
Deaf	2.3	6.9
Hard of hearing	5.3	5.5
Cardiac	7.7	10.9
Dwarf	0.3	0.4
Diabetes	0.1	...
Epilepsy	0.1	...
Tuberculosis (pulmonary)	5.4	5.2
Pulmonary disease other than tuberculosis	0.6	...

* One disability, 91.7 per cent of impaired sample; two disabilities, 7.6 per cent of impaired sample; three disabilities, 0.7 per cent of impaired sample.

† Less than 0.05 per cent.

Tuberculosis was listed as a defect in 5.4 per cent of the physically impaired males and in 5.2 per cent of the females. These cases included pulmonary tuberculosis, arrested according to National Tuberculosis Association standards. The majority were minimal in type; 10 per cent of these workers were reported to be receiving collapse therapy or to have undergone, in the past, operative procedures for permanent collapse.

A small miscellaneous group of defects, including dwarfism, diabetes, epilepsy and pulmonary disease other than tuberculosis, were reported in the study; these defects were found in 1.1 per cent of the male physically impaired workers and in 0.4 per cent of the female.

(To be continued)

EPIDERMAL AND DERMAL SENSITIZATION

(COEXISTING IN THE SAME INDIVIDUAL)

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The clinical pictures of epidermal sensitization and dermal sensitization and the mechanisms of their production are well known to students of these problems. In their pure forms they constitute separate entities.

When the epidermis alone is sensitized it has generally been brought into this state of sensitization by previous contact of its surface with some external agent capable of producing sensitization. Such an agent may have been either a primary cutaneous irritant or a cutaneous sensitizer. The resulting clinical picture is known by the old name dermatitis venenata or the newer term contact dermatitis. It might well be called "epiderma-titis" because this term accurately describes the location of the shock tissue, which is the epidermis.

When the dermis alone is sensitized, the offending substance, the allergen, has generally reached it from within the body by way of the blood vessels or lymphatics. The allergen will generally have entered the body by way of inhalation or ingestion. Sometimes, however, it arises from substances elaborated within the body and, more rarely, by means of transepidermal absorption. The reaction of the sensitized dermis to allergens coming in contact with it expresses itself morphologically in different forms such as toxic erythemas, urticaria, erythema multiforme and various forms of dermatitis. Among the latter is that form of flexural dermatitis known under various names as neurodermatitis or atopic dermatitis. All of these represent reactions of the shock tissue, the dermis, and constitute true "derma-titis."

While in most instances these two processes are separate and distinct entities there are many times when the one process merges into the other, when both the epidermis and the dermis are sensitized. It is my purpose in this paper to discuss such cases from the clinical and pathogenic points of view.

EPIDERMAL AND DERMAL SENSITIZATION FROM DRUGS

Probably the most frequently seen examples of epidermatitis and dermatitis coexisting in the same patient are from sensitization to drugs:

Mrs. H., aged 35, consulted me because of severely edematous dermatitis of the scalp and face following the use of a new hair tonic. These areas rapidly developed the type of dermatitis that is so characteristic of epidermal involvement, i. e. a fine pebbly superficial vesiculation, which went on to oozing and crusting. This hair tonic was found to contain chloral hydrate, and a patch test to this substance was strongly positive. Under conservative treatment the dermatitis entirely disappeared. Three years later another physician prescribed chloral hydrate as a sedative. Within a few hours after ingestion of the first dose the patient noted pebbly, vesicular dermatitis of the scalp and face. At the same time extensive areas of typical urticaria developed elsewhere on the body. This could mean nothing but dermal sensitization also.

This case represents an example of epidermal sensitization from surface application of a drug. Later when the drug was taken by mouth enough of it reached the sensitized epidermis, from within, to produce a severe recurrence. The fact that the dermis had also become sensitized was evidenced by the urticaria.

Mrs. L., aged 40, came under my care because of a recalcitrant pustular eruption of the palm. Her former physician reported that dermatitis venenata of the palm developed following the use of sulfathiazole ointment. After this phase of her trouble had entirely subsided the same ointment was inadvertently used again, with the result that the dermatitis venenata immediately returned. This disappeared. Several weeks later, because of the spreading of the pustular element over the hand, sulfathiazole tablets were prescribed to be taken by mouth. Within an hour following the ingestion of the first 7½ grain (0.5 Gm.) tablet the palm and hand became swollen and edematous. The drug was discontinued. By the next day there were many evanescent lesions typical of urticaria scattered over the body.

This again is an example of epidermal sensitivity to a drug applied to the skin, followed later by a second attack produced by ingestion of the same drug and associated with a dermal sensitization reaction (urticaria).

Miller [1] reported an almost identical reaction to sulfathiazole given by mouth six months after this drug had produced dermatitis when used as an ointment. Such examples are now of almost everyday occurrence. There are no better examples of the phenomenon of epidermal and dermal sensitization existing in the same individual than those which follow the external application of the various sulfonamide drugs. These drugs are powerful sensitizers and, when applied externally, indiscriminately, in the form of ointments, proprietary combinations, nasal sprays, nose drops and ophthalmic ointments, all too frequently set in motion the mechanism of double sensitization. The fact that they sensitize the epidermis to future external applications is bad enough, but the frequently associated dermal sensitization is far more serious in that it deprives the patient of the use of a valuable internal remedy in case of grave systemic infections in the future.

That epidermal sensitization, as well as dermal sensitization, takes place occasionally following the internal administration of arsphenamine is proved by those patients who react with a vesicular reaction to patch tests to arsphenamine solution following attacks of arsphenamine dermatitis.

EPIDERMAL AND DERMAL SENSITIZATION FROM PLANTS

Sensitization of the epidermis to poison oak is extremely common. In nearly all instances such sensitization arises from external contact with the plant. However, the common practice of giving poison oak extract by mouth or by injection as a prophylactic or therapeutic measure occasionally furnishes us with examples of combined epidermal and dermal sensitization.

Some time ago I pointed out [2] that the hypodermic injection of poison oak extract into patients already suffering from poison oak epidermatitis occasionally produced a generalized urticarial (dermal) reaction. I have seen the same urticarial reaction following the

Read before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 16, 1944.

1. Miller, J. Lowry: Use of Sulfanilamide and Its Derivatives in Ointment Form, Arch. Dermat. & Syph. **46**: 379 (Sept.) 1942.
2. Templeton, H. J.: Untoward Reactions Following Toxin Treatment for Dermatitis Venenata, Arch. Dermat. & Syph. **20**: 83 (July) 1929.

oral ingestion of poison oak extract. Such cases are excellent examples of combined epidermal and dermal sensitization. There is little doubt that the same phenomenon could occur from other sensitizing plants such as primrose.

Fivoli[3] reported a case of dermatitis of the back of the hands from picking camomile in which a positive patch test indicated epidermal sensitivity. An anaphylactic attack following oral ingestion of a decoction and a positive passive transfer test with vesicle fluid indicated systemic sensitization.

EPIDERMAL AND DERMAL SENSITIZATION TO FOODS

Examples of patients who develop epidermatitis from external contact with foods and also dermal reactions such as urticaria or atopic dermatitis ffom the ingestion of that same food are relatively rare. I have seen only a few such cases in my own practice but have been able to gather together some from the files of my colleagues.

A girl aged 22 months had had eczema of the face, the arms and the cubital and popliteal spaces since the age of 6 months. Clinically this was typical neurodermatitis. The ingestion of egg had repeatedly produced an exacerbation of this condition. Removal of egg from the diet helped but did not entirely cure the condition. The mother reported that, whenever egg white touched the skin, dermatitis appeared within a few minutes. I had her repeat the experiment (as an equivalent of a patch test) and the resulting dermatitis had, to me, the clinical appearance of epidermatitis.

Deissler[4] reports:

I found, somewhat to my surprise, that we seem to have only 1 case on record in which double sensitization was actually proved. A man in his early thirties, working in an Italian sausage factory, had hay fever and eczema in childhood. His mother had asthma. In mixing the sausage dough he handles daily large quantities of sausage mix which contains in solution among other things casein and wheat flour. Such contact will produce a dermatitis on exposed areas but no other symptoms. However, the eating of either wheat or milk will produce a papular skin lesion and severe asthma. This sequence of events has been tested by repeated exposing and withholding. Patch tests to milk and wheat were positive.

Rowe[5] reported the following case to me:

I. C., a woman whose brother has hay fever, developed dermatitis of the hands which was proved to the satisfaction of the physician and the patient to be due to the ingestion of tomatoes. The patient reproduced this condition by experimentally eating tomatoes. After her dermatitis had entirely disappeared she reproduced epidermatitis of the hands by peeling and slicing tomatoes without eating any.

Urbach[6] reported the case of an 18 year old girl with papular urticaria. Withdrawal of lemon controls the disease, ingestion of lemon juice or skin of lemon provokes severe pruritus and urticaria. A vesicular reaction to a patch test with lemon proved that epidermal sensitivity also existed.

Mauser[7] reports the following case:

A boy aged 2 years, with a history of atopy on both sides of his family, developed swelling of the face around the eyes almost immediately following the ingestion of eggs; this reaction disappeared in three or four hours (dermal type of sensitization). This phenomenon was repeated experimentally several times following the ingestion of eggs. The white of egg seemed to produce the worst reaction. He has inadvertently had eggs in food several times with the same result. A scratch test to egg gave a 3 plus reaction. Application of egg or egg shells to the face caused a swelling and blotching of the face immediately at the site of contact lasting for an hour.

The rapid appearance and disappearance of the dermatitis following contact of the skin with egg probably represents an example of transepidermal absorption and a resulting epidermal-dermal reaction rather than an uncomplicated epidermal reaction.

Mrs. K. B., aged 30, was treated for a dermatitis of the hands and face which was thought, clinically, to be a contact dermatitis. However, at the same time she suffered from rather typical neurodermatitis of the flexures and the neck. After long observation it was found that the contact dermatitis of the hands occurred after handling wheat flour and that one of the causal factors in her neurodermatitis was related to the ingestion of wheat.

EPIDERMAL AND DERMAL SENSITIZATION FROM AUTOGENOUS PRODUCTS

That type of dermatitis in which the epidermis and dermis around the site of chronic irritation (for example, leg ulcers) becomes sensitized to the local discharges, which process is followed after varying intervals of time by a severe generalized dermatitis of the toxic or urticarial type, is a good example of combined sensitization. For example, a patient will give the history of having a leg ulcer for a long time. He will have noticed that the serous discharge from the ulcer has superficially irritated the skin around the ulcer (epidermal reaction). Then suddenly a toxic erythema or urticaria will have developed, with explosive violence, over his whole body. This process, which I have seen in scores of patients, is an example of what Whitfield[8] aptly named "autosensitization." In it the patient's epidermis probably first becomes sensitized to his own altered tissue proteins or to bacterial antigens produced by contaminating infection. In due time enough of these autogenous products become absorbed to sensitize his whole dermis (and epidermis?) to them and then a violent dermal reaction results from the blood or lymph borne allergens. As a related example, I was called in consultation to see a patient with a severe generalized toxic erythema and evanescent urticarial lesions. He gave the history of having received a second degree burn about three weeks previously, which involved the right side of his chest. A week after the accident typical vesicular epidermatitis appeared around the burn at the site of application of butesin picrate ointment. Eight days later the toxic erythema and urticaria appeared over his entire body.

This patient presented both epidermal and dermal reactions. It seemed quite evident that the original epidermatitis was caused by the butesin picrate, but it is difficult to say whether the allergen which produced the generalized dermal reaction was butesin picrate, burned tissue proteins or a combination of the two. I have seen a number of cases identical in mechanism with this one.

COMMENT ON MECHANISM OF PRODUCTION

Combined epidermal and dermal sensitization may occur from allergens reaching the skin from without or from within. In my experience the primary sensi-

3. Fivoli, C.: Hypersensitivity to Camomile, Dermatosifilografo **11:** 614, 1936.
4. Deissler, Karl J., Oakland, Calif.: Personal communication to the author.
5. Rowe, Albert H., Oakland, Calif.: Personal communication to the author.
6. Urbach, Erich, Philadelphia: Personal communication to the author.
7. Mauser, Carl L., Oakland, Calif.: Personal communication to the author.
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tization has nearly always been from allergens applied to the surface of the epidermis. Dermal sensitization has been secondary to the epidermal involvement. This concept implies that the dermis has become sensitized to exogenous materials that must have penetrated unchanged through the epidermis to reach the deeper layers or that the dermis has become sensitized to inflammatory products formed in the epidermis consisting of a union of the offending externally applied allergen and the tissue protein of the epidermal cells.

The first of these theories, that of transepidermal absorption as the route of dermal sensitization, is easy to accept, as transepidermal absorption of drugs, plants and allied substances is well known. One of the oldest examples is that of the absorption of mercury from inunctions. Macht [9] has shown that plant substances such as essential oils are easily absorbed through the intact epidermis. It has been demonstrated by Walzer [10] that proteins can penetrate the epidermis to produce a positive allergic reaction in a remote area of the skin previously sensitized by intracutaneous injection of the same protein. It can be shown both experimentally and clinically that endocrine substances such as testosterone are absorbed through the epidermis. Sulzberger has demonstrated transepidermal penetration.

The second idea, that of the dermis becoming sensitized to a chemical-epidermal protein product, is more difficult to prove or illustrate. Dennie [11] felt that this was what happened when an originally localized picric acid dermatitis became generalized over the body. He spoke of the absorbed allergen as a "protein-picrinate."

As stated previously, Whitfield [8] has demonstrated that the epidermis may become sensitized to products of cutaneous irritation such as vesicle fluid and react with epidermatitis when this fluid trickles over the skin. Every dermatologist has seen numerous examples of dermal reaction (toxic erythema and urticaria) from the absorption of altered tissue proteins from ulcers and burns, named by Whitfield "autosensitization."

Examples of combined epidermal and dermal sensitization in which the dermis was first sensitized from endogenously applied substances do exist, in my opinion, but are rare. In such cases the dermis would probably have to have been sensitized first by allergens reaching it by the blood stream and then the epidermis would have become secondarily sensitized by absorption of products from the altered dermis.

In those patients who develop epidermatitis from handling a certain food as well as some dermal reaction from eating it, it is impossible to be certain of the mechanisms involved. The epidermis may have become sensitized by contact with the food and the dermis, independently, from its ingestion. We also have to consider the possibility of both structures having been initially sensitized ab externis, but it seems to me that the most likely possibility is that they have both become sensitized ab internis following ingestion.

SUMMARY

Although epidermal and dermal sensitizations are quite well known as distinct entities, little has been written concerning the combinations of the two processes. Probably the most important of these combined sensitizations which we are seeing today are those resulting from topical applications of drugs, particularly the sulfonamides. Since the sulfonamides so used are powerful cutaneous and systemic sensitizers, their indiscriminate use in ointments, sprays and powders should be discouraged.

3115 Webster Street.

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10. Walzer, Abraham: Cutaneous Absorption, Arch. Dermat. & Syph. **41**: 692 (April) 1940.
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ABSTRACT OF DISCUSSION

DR. EDWARD A. OLIVER, Chicago: Before any of the numerous reports on sulfathiazole sensitization had been published I learned a valuable lesson. A patient of mine consulted me for the treatment of several large furuncles on one leg. They were a peculiarly resistant type of lesion, and one day at the insistence of a druggist friend he applied sulfathiazole powder to his leg. The skin became badly irritated, but eventually it cleared up and the furuncles disappeared. Three months later he appeared with several new furuncles of the same resistant type. I advised him to go home, apply warm boric acid compresses to the parts and prescribed sulfathiazole tablets 0.5 Gm. to be taken four times daily. After he had taken the second tablet his face became swollen, his hands and feet began to itch and burn, subsequently numerous vesicles and bullae appeared on these areas, and he developed a generalized toxic erythema of the entire body. This, I consider, a typical case of combined epidermal and dermal sensitization. These cases are reported quite commonly now. I have seen intense flare-ups develop during the treatment of rhus dermatitis following the therapeutic injection of rhus antigen, and, while I have seen no examples of sensitization from external contacts with foods in patients who have developed urticaria of atopic dermatitis from ingestion of that food, one of my friends, a pediatrician, has told me that 2 babies with infantile eczema in which he found a distinct allergy to eggs were completely relieved from their eczema when eggs were removed from the house. There is a distinct odor emanating from eggs, and he is convinced that epidermal sensitization occurred through inhalation. As to the case of butesin picrate sensitization, I am inclined to believe that the generalized dermal reaction is due to butesin picrate alone. In patients allergic to that material I have seen most annoying generalized toxic dermatitis develop after the use of butesin picrate on minor injuries, cases in which there was no possibility of toxic products at the site of the wound being responsible. I feel that Dr. Templeton's explanation of the mechanism of this sensitization is a satisfactory one.

DR. ADOLPH ROSTENBERG, Washington, D. C.: The late Dr. Karl Landsteiner did a tremendous amount of work on the mechanism of sensitization and studied the production of sensitization by the simple application of surface chemicals, then determining whether sensitization was simultaneously induced in shock tissues other than the epidermis. In brief he found that the simple cutaneous application of chemicals such as dinitrochlorobenzene and picryl chloride often simultaneously caused the development of the anaphylactic type of sensitivity as well as the epidermal eczematous type. Landsteiner conjugated his chemicals with various proteins. Now he injected those protein conjugates intravenously and found that the animals would often die in anaphylactic shock and that this state had been induced by the mere surface application of the simple chemical. Ordinarily the substances we meet as contacts (and which are capable of eliciting an eczematous sensitization) are not taken internally. The sulfonamides, as has been mentioned, are a more or less notorious exception to this. Fortunately we don't ordinarily imbibe nickel or paraphenylenediamine or meet them as conjugates. These simple chemicals may cause varieties of sensitization in addition to the epidermal, but for the nonepidermal varieties they act similarly to what we call a hapten, although I am not using this word in its technically correct sense. As simple chemicals they are able to elicit or cause the reaction only in the epidermis, but if they have the opportunity to conjugate and act as the hapten of the conjugate it is then that we get the reaction in the other shock tissues. It may be,

as has been mentioned here, that when there is infection present concomitantly with an epidermal sensitization it favors the production of conjugates; in fact, there has been some experimental work done by Haxthausen of Copenhagen to show this. Accordingly, I think the phenomena that Dr. Templeton mentions may be a little more common than we ordinarily realize. We in the Food and Drug Administration are much concerned with the indiscriminate use of the sulfonamides. I think it would be an act of public service if this section would go on record as condemning the promiscuous use of the sulfonamides for banal dermatoses.

DR. CHARLES C. DENNIE, Kansas City, Mo.: Dr. Templeton mentioned my name in reference to some of the original work done along this line. The work was done in 1929 on the mechanism of sensitization. The experiments were carried out as pure experimental procedures concerning the effect of picric acid on the uninjured human skin. We found that 4 per cent of all individuals that we tested were sensitive to this material, and that 2 of these cases developed very queer phenomena, in that not only did they secure a local reaction but this reaction spread up through the lymphatics into the general blood stream. The patients developed a severe generalized dermatitis which put 1 of them in the hospital for several weeks. We then carried out some experiments on dogs. We tested them with picric acid. Under proper chemical procedures we ground up the skin and leached with alcohol to remove the picric acid, dialyzed the ground-up skin and were able to split the picric acid from the protein. It was my opinion that the protein might form a basis for the sensitization and that the sensitization occurred primarily not because of the picric acid but because of the proteins that had been broken off from the picric acid so that the former was again available for producing new protein picrinate. This process kept up for a long time. We found that the picric acid in the system was excreted very slowly. We could demonstrate the picric acid in the urine and in the blood after a certain length of time. I have worked a good deal on that concept since then. There is no doubt that double sensitization takes place. I just want to report 1 case of a medical officer who was a resident surgeon in the Kansas City General Hospital. He became sensitized to rubber gloves. He was forced to give up surgery. He was then inducted into the Army Air Forces. The first time he put on a gas mask he broke out on his face very badly. The second time he put on the gas mask the original areas on the backs of his hands broke out in all of their former intensity.

DR. HOWARD FOX, New York: I don't agree with the statement that nothing can be done through publicity to stop the indiscriminate local use of sulfonamide drugs. I think something can be done by calling attention to this subject frequently. A resolution from this section of the American Medical Association would certainly carry weight with the medical profession. Such a resolution should refer to the present indiscriminate local uses of sulfonamide drugs by physicians and the fact that these drugs are often used in cases in which safer drugs are equally efficacious.

DR. JOHN G. DOWNING, Boston: There is an industrial aspect to this type of sensitization. I recently treated an expert pastry cook who suffered a dermatitis not only from external contact to the eggs mixed with pastry flour but also to the ingestion of eggs. He showed positive skin tests to the powdered egg. I have seen similar instances in salad makers who are sensitive not only to the contact with the lettuce but also to the ingestion of this substance. This also happens in workers exposed to tomatoes and fish.

Medieval Medicine.—In medieval medicine the onion was held in highest regard, an idea later revived by Sydenham, who recommended the vegetable for use in smallpox. Lord Bacon believed that the odor of onions would sustain life in the absence of food and water; while Nicolas Lemery, one of the most celebrated chemists of the seventeenth century, wrote that water in which garlic has been steeped has the power of shattering glass. Lind, the conqueror of scurvy in the British Navy, held that "vinegar and garlic are no contemptible preservatives in times of infection."—Gordon, Benjamin Lee: The Romance of Medicine, Philadelphia, F. A. Davis Company, 1944.

Clinical Notes, Suggestions and New Instruments

EFFECT OF THE ADMINISTRATION OF CHOLINE CHLORIDE ON THE HEMATOLOGIC PICTURE IN HUMAN BEINGS

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Davis[1] recently reported that the administration of choline chloride orally to dogs in a dose of 10 mg. per kilogram of body weight three times a day for several months resulted in the development of a macrocytic hyperchromic anemia. The anemia responded to anti-pernicious anemia liver extract, ventriculin and atropine sulfate although the reticulocytes rose during therapy only 1.5 to 2.3 per cent. Davis advances the theory that choline depresses erythropoiesis by increasing the blood and oxygen supply to bone marrow through its vasodilator action.[2]

Results of the Blood Studies on Three Patients Receiving Choline Chloride in a Dose of 30 Mg. per Kilogram Daily

Patient	Days of Experiment	Red Blood Cells, Millions per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Hematocrit, Cc. per 100 Cc.	Mean Corpuscular Volume, Cubic Microns	Mean Corpuscular Hemoglobin, Micromicrograms	Mean Corpuscular Hemoglobin Concentration, per Cent	White Blood Cells, per Cu. Mm.
E. C.	0	5.77	14.8	47.5	82	26	31	8,800
	30	5.86	15.4	51.0	87	26	30	7,250
	60	5.64	15.4	49.0	87	27	31	9,000
	90	5.44	15.0	47.0	87	27	32	12,100
H. B.	0	4.90	14.7	44.0	90	30	34	9,100
	30	5.30	14.9	47.0	89	28	31	9,550
	60	5.46	16.0	47.8	88	29	33	9,400
	90	5.37	14.2	48.0	89	26	30	12,800
C. D.	0	5.57	14.3	46.0	83	26	31	8,300
	30	5.73	14.4	49.1	86	25	29	6,500
	60	5.87	14.7	50.0	85	25	29	5,220
	90	5.80	14.5	49.5	85	25	29	7,400

The implications of this experiment are extremely important[3] and for this reason it seemed desirable to ascertain the effect of the administration of choline on the blood of human beings.

PROCEDURE

Three men were used. One (E. C.), aged 47, was suffering from multiple sclerosis. The second (H. B.), aged 75, had a hemiplegia of several years' duration due to a cerebral vascular accident. The third (C. D.), aged 60, had generalized arteriosclerosis. The patients were given approximately 30 mg. per kilogram of body weight of choline chloride orally per day. This was made up in an aqueous solution and given in divided doses at 8 a. m., 1 p. m. and 6 p. m. daily for ninety days. The hematologic determinations were done according to the methods of Wintrobe.[4]

The results are presented in the accompanying table.

CONCLUSION

Choline chloride given in doses of 10 mg. per kilogram of body weight orally three times daily to 3 adult human males for ninety days failed to produce either anemia or macrocytosis.

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From the Department of Medicine, University of Utah Medical School.

1. Davis, J. E.: Am. J. Physiol. **142:** 402 (Oct.) 1944.
2. Davis, J. E.: J. Pharmacol. & Exper. Therap. **70:** 408 (Dec.) 1940; Am. J. Physiol. **142:** 65 (Aug.) 1944.
3. Experimental Hyperchromic Anemia, editorial, J. A. M. A. **127:** 223 (Jan. 27) 1945.
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COUNCIL ON PHARMACY AND CHEMISTRY

REPORT OF THE COUNCIL

For over fifteen years poison ivy preparations have been included in New and Nonofficial Remedies. There is evidence that people sensitive to poison ivy can be desensitized temporarily by the use of such preparations, but the method requires expert supervision and the careful selection of patients because of possible unfavorable reactions. On the basis of evidence available to it, the Council is of the opinion that the extract may be made by extracting the fresh twigs or leaves of Toxicodendron radicans, diversilobum or quercifolium, dried rapidly at a low temperature immediately after collection, then extracted in absolute alcohol, ether or acetone; the extract, solid or liquid, should be standardized for potency by determining the weakest solution or dilution which will give a positive patch test in from 50 to 60 per cent of an average sample of the normal adult exposed population; this solution or dilution should be used as a reference standard for the preparation of a series of doses graded in increasing strengths for parenteral injection, the initial dilution or solution being one which will not give a patch reaction in any sensitive subject; and no claim for treatment of the acute dermatitis should be allowed.

Dr. Franklin A. Stevens has prepared for the Council a review of the status of poison ivy preparations. This report, which has been adopted for publication, should be especially useful to the general practitioner.

AUSTIN SMITH, M.D., Secretary.

STATUS OF POISON IVY EXTRACTS

FRANKLIN A. STEVENS, M.D.
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The Council on Pharmacy and Chemistry admitted rhus preparations to New and Nonofficial Remedies in 1926. This recognition was based chiefly on the favorable reports of Schamberg,[1] Strickler,[2] Alderson,[3] Bivings[4] and Williams and MacGregor,[5] all of whom believed that patients with "rhus dermatitis" were remarkably benefited by the administration of the extracts. In 1926 the classification of species of poison ivy was in confusion, very little was known about the chemistry of the irritant causing the dermatitis, and knowledge of its mode of action and of the mechanism of the immunity induced by the administration of the extracts was meager. Subsequent botanic, chemical and immunologic studies have solved some of these problems. On the other hand, there has been a growing controversy regarding the real value of rhus preparations. In spite of contradictory clinical reports showing a real division of opinion on the subject, accepted brands of poison ivy, oak and sumac extracts have been carried continuously in New and Nonofficial Remedies since 1926. The favorable results obtained therapeutically by some clinicians could not be entirely discounted.

CLASSIFICATION OF SPECIES OF POISON IVY: THE MORPHOLOGIC SIMILARITY OF THE SPECIES

Botanists have described about fifty species of poison ivy native to North America.[6] Since the chief point of differentiation has been the shape of the leaflets, which vary greatly in contour in different plants and sometimes in the same plant of any of the species, it is not surprising that the species described have been so numerous. The terms "poison vine," "ivy" and "oak" have been used to describe plants of any species if they had vinelike or shrublike characteristics or had a tendency to grow like a tree. On the other hand the term "poison oak" is also used to designate certain species with indented oaklike leaves. When Warren[7] enumerated the poisonous species of the genus Rhus and of the parent family, he stated specifically that many of the synonyms and subvarieties had been omitted. To avoid the confusion caused by the use of synonyms given the same species in different classifications, Spain[8] employed the classification of Kuntze as adopted by the United States Herbarium in Washington, D. C. According to this classification Rhus toxicodendron (L) or Rhus quercifolia (Steud.) becomes Toxicodendron toxicodendron (L) Britton. The term Toxicodendron radicans (L) Kuntze is given to the eastern ivy. The western poison oak, Rhus lobata (H) or Rhus diversiloba (T. and G.), is known as Toxicodendron diversilobum (T. and G.) Greene. The poison or swamp sumac, Rhus vernix (L) or venenata (D. C.), is classified with the ivies as Toxicodendron vernix (L) Kuntze. Recently Shelmire[6] transplanted plants representing three species of ivy from their normal habitat to Texas, where they were grown under similar physical conditions. After observing the growth of these plants, he concluded that T. toxicodendron (L) (quercifolium [Steud.]), T. radicans (L) and T. diversilobum (T. and G.) should be treated taxonomically as a single pleomorphic species with more or less consistent geographic variations.

When extracts of ivy were first popularly employed therapeutically, the proponents of the therapy considered the species of ivy distinct botanically and biologically. Unfavorable results were sometimes attributed[9] to differences in species.[10] Possibly for these reasons extracts of ivy, oak and sumac were accepted by the Council. From chemical and biologic evidence available today, it seems most probable that the same chemical substance is the active agent in the saps of the poisonous varieties of ivy, oak, sumac and the lac trees. Until convincing contradictory evidence is brought forth, it is believed that a single extract can be used in the prophylaxis of the dermatitis caused by contact with any one of these plants. The evidence supporting this belief is found in succeeding paragraphs.

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2. Strickler, A.: Toxin Treatment of Dermatitis Venenata, J. A. M. A. **77**: 910 (Sept. 17) 1921; footnotes 69 and 70.
3. Alderson, H. E.: California & West. Med. **23**: 982, 1925. Alderson and Pruett.[71]
4. Bivings, F. L.: Successful Desensitization and Treatment of Poison Ivy and Poison Oak Poisoning, Arch. Dermat. & Syph. **9**: 602 (May) 1924.
5. Williams, C. M.: M. J. & Rec. (supp.) **119**: 131, 1924. Williams, C. M., and MacGregor, J. A.: Treatment of Ivy Poison by Rhus Tincture and Antigen, Arch. Dermat. & Syph. **10**: 515 (Oct.) 1924.
6. Shelmire, B.: J. Invest. Dermat. **4**: 337, 1941.
7. Warren, L. E.: Pharm. J. **83**: 531, 1909.
8. Spain, W. C.: J. Immunol. **7**: 179, 1922.
9. Morrow, H.: Poison Ivy Treatment, Arch. Dermat. & Syph. **11**: 266 (Feb.) 1925.
10. Schamberg, J. F.: Poison Ivy Treatment, Arch. Dermat. & Syph. **11**: 266 (Feb.) 1925.

URUSHIOL: THE ACTIVE SUBSTANCE COMMON TO THE POISON IVIES, POISON SUMAC AND THE LAC TREES

Poisoning by ivy was first thought to be due to an emanation from the plant. According to Thompson (quoted from McNair [11]), the North American Indian and the Negro shared in this belief. The Japanese and Chinese apparently had a similar conception concerning the toxic effects of the lac trees (quoted from Toyama [12]) because they believed that people passing them could be poisoned. Influenced by these impressions and probably by the hard dying doctrine of the middle ages that disease was caused by vapors, most chemists of the eighteenth and nineteenth centuries directed their attention to a search for a volatile poison. Their opinions were divided on this question, and now their observations have no relevant bearing on the modern chemistry of the poisonous factor in ivy.

In 1897 Pfaff [13] published the results of a chemical study of the irritant of Rhus toxicodendron (L) and venenata (D. C.). An oily material was extracted from the plants with alcohol and precipitated as a lead compound ($C_{21}H_{30}O_4Pb$). It was called toxicodendrol. This substance was nonvolatile, insoluble in water, soluble in alcohol and lipid solvents and caused dermatitis. Between 1905 and 1909 Tschirch and Stevens,[14] Stevens,[15] Stevens and Warren [16] and Warren [7] obtained clear stable "oils" which they believed were identical from the saps of the Japanese lac tree, of sumac and of poison ivy. McNair [17] later undertook a similar study of western poison oak (Rhus diversiloba [T. and G.]). By successive extractions through alcohol, petroleum ether and alcohol, he obtained a material called "lobinol." The dermatitis occurring when lobinol was applied to the skin was similar to that following exposure to poison ivy. It was thought to be an unsaturated compound of the aromatic series, polyphenolic in character with two hydroxy groups in the orthoposition. Further analysis was not done. These investigators isolated similar substances from ivy, lac and sumac and oak but failed to prove that the compounds were identical.

In 1907 Majima and his associates [18] undertook a chemical study of the active substance in Japanese lacquer. This lacquer is the sap of Rhus vernicifera, the Japanese lac tree, and is called "kiurushi." The investigation extended over more than a decade. They isolated a nonvolatile oil soluble in alcohol, benzene, chloroform, petroleum ether and so on. It was a skin irritant. This oil, called urushiol, proved to be a mixture of o-dihydroxy benzene derivatives with a normal fifteen carbon side chain with two unsaturations. The different components varied only in the number and position of the double bonds. There were two unsaturated fractions with two double bonds, some fully saturated oil (hydrourushiol) and probably a fraction with more than two unsaturations. None of the components could be separated by distillation, and all on reduction formed 1, 2 dihydroxy, 3n-pentadecyl benzene. The dimethyl ether of this substance was synthesized. Toyama [12] believed that urushiol and the toxic oil from ivy were identical, but no further chemical study of ivy extracts was made until 1934. Then Hill, Mattacotti and Graham [19] published analyses of derivatives of a substance obtained by the extraction of the bark of Rhus toxicodendron with alcohol. The alcoholic extract was evaporated and the residue extracted with xylene. The oil obtained had the same molecular weight, boiling point and analysis as urushiol. Since the unsaturated dimethyl ether, the reduced substance and the dimethyl ether, diacetate and dibenzoate of the solid obtained by reducing the oil extracted from ivy had the same constants as similar derivatives of urushiol, the oils from Japanese lacquer and from ivy were believed to be identical. The accepted formula for this benzene compound is $C_{21}H_{32}O_2$. It is fluid and boils at 210 degrees (0.4-0.6 mm.), if unsaturated, but on reduction precipitates. Hydrourushiol, the reduced substance, is soluble in the unsaturated component.

THE OXIDATION OF URUSHIOL: LACCASE, THE CATALYZING ENZYME

Darkening, precipitation and loss of toxicity occur when the saps of poison ivy, swamp sumac and lac trees are exposed to the air. These physical changes are the result of oxidation, rearrangement of the molecular structure and an aggregation or condensation of the molecules of oxidized urushiol. Oxidation, which proceeds rapidly in warm moist air, is catalyzed by laccase, a blue copper-protein enzyme first investigated by Yoshida [20] (from Rhus vernicifera [L], Japanese lac tree) and subsequently by Bertrand [21] (from Rhus succedanea [L], Indo chinese lac), Stevens and Warren [16] (Rhus vernix [L]), Suminakura,[22] McNair [23] (from Rhus diversiloba [T. and G.]) and by Keilin and Mann [24] (from Rhus succedanea [L]). This enzyme is insoluble in ether and is precipitated by approximately 50 per cent acetone but requires stronger solutions of alcohol. It is said the enzyme is still active in 50 per cent ethanol. If the enzyme is destroyed or urushiol is isolated free from the catalyst, oxidation may occur spontaneously but very slowly if water is present. Spontaneous oxidation is enhanced in alkaline solutions. Orthophenols and paraphenols are first oxidized to the corresponding quinones. Experiments with derivatives of urushiol seem to indicate that its toxicity depends on the integrity of the hydroxyl groups. Hill, Mattacotti and Graham [19] and Toyama,[12] although not in perfect agreement as to the degree of detoxification, discovered that reduction slightly lessened the toxicity of urushiol, monomethylation or dimethylation rendered it almost or completely inert, and dimethyl hydrourushiol was nontoxic. In 1917 McNair,[23] familiar with the work of Yoshida and of Bertrand, studied an enzyme from R. diversiloba (T. and G.). It was similar to the one isolated by Keilin and Mann because it catalyzed the oxidation of orthophenols and paraphenols and of paraphenylenediamine. McNair hesitated to attribute the gradual loss of toxicity, which

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17. McNair, J. B.: J. Am. Chem. Soc. **38**: 1417, 1916; **43**: 159, 1921; footnote 11.
18. Majima, R., and others: Ber. d. deutsch. chem. Gesellsch. **55**: 172, 1922. Majima, R., and Nakamura, I., ibid. **48**: 1597, 1915.
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21. Bertrand, G.: Compt. rend. Acad. d. sc. **118**: 1215, 1894.
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24. Keilin, D., and Mann, T.: Nature, London **143**: 23, 1939; **144**: 140, 1940.

occurs simultaneously with the darkening of rhus sap to the catalyzing properties of laccase.

The physical and chemical properties of urushiol are such that many beliefs concerning poison ivy dermatitis are found untenable and at the same time other common observations are fortified. One old and prevalent idea held by excellent authority [25] even as late as 1934,[26] that the poison could be wind borne, has never been confirmed by any chemical or physical study of the properties of urushiol. The only identified volatile substance found in the sap in any quantity is acetic acid,[27] which was once isolated, wrongly identified, called "toxicodendric acid" and believed to be the toxic chemical.[28] On the other hand, it appears that enough oil can be carried on soot particles [29] in the smoke [30] from burning plants to cause dermatitis in sensitive people and that sufficient amounts will adhere to dust particles in shops where lacquer is used and be carried out in drafts to give dermatitis to passers-by.[12] These observations are understandable since it is said that 0.001 mg. of urushiol will cause dermatitis in very sensitive people.[16] Although never proved, the concept that insects feeding on the broken leaves may be transmitting agents seems plausible. There is no doubt that animals, tools and contaminated clothing act as conveyors. Apparently thick deposits of dried sap on clothing,[31] the lacquer on varnished articles [12] and lacquer dried in mass resist complete oxidation for months and possibly for centuries.[12] The outer hardened shell presumably protects inner layers from moisture and air and prevents complete oxidation. McNair [23] observed that demonstrable oxidation of very thin films of sap on glass continued in moist air for at least a month.

The solubilities of urushiol and its laccase in various solvents account for some of the variations in the potency and stability of different therapeutic extracts. Although pure urushiol has been considered stable, in slightly alkaline solution it oxidizes slowly spontaneously and rapidly if laccase is present even if slightly acid. Spain [8] used extracts of fresh leaves made by covering the leaves with 95 per cent alcohol. The proportions were not stated. These precipitated. Subsequently [32] 1 Gm. of fresh leaf was covered with 3 cc. of alcohol; later absolute alcohol was used and finally, to obtain a stable product, the leaves were dried before immersion in absolute ethanol. Spain and Cooke [32] thought that deterioration may have been caused by chlorophyllase, an alcohol soluble enzyme, and so dried the leaves and then extracted them with absolute alcohol to avoid traces of water. Their extracts of fresh leaf contained, according to the author's calculation, approximately 15 to 20 per cent of water. Laccase is said to be active in 50 per cent ethanol; whether it will act in stronger concentrations appears not to be stated in the literature. Since a black precipitate settled out of their concentrates made from fresh leaves, it is possible that laccase was present and active in these extracts. From extracts of dry leaves evaporated in the absence of oxygen, they obtained a clear oily substance active in dilutions of 1 to 100,000. They found this substance stable. Acetone and ether were later used as extractives of fresh leaves and twigs. Fifty per cent solutions of acetone precipitate laccase and dissolve urushiol. However, ether will dissolve this substance without extracting laccase from fresh material. It appears from the chemistry and solubilities of urushiol and the associated polyphenolase that the laccase must be inhibited from acting from the time the leaves are broken and the natural inhibition ceases until the oil is separated from the catalyst in a suitable differential solvent. This end might be accomplished if leaves which had been macerated with solid carbon dioxide were dried while frozen and then extracted with ether.

SENSITIVITY TO POISON IVY EXTRACTS: CLINICAL ASPECTS

All observations indicate that ivy dermatitis occurs only after a person has been exposed and sensitized. Sensitization to Toxicodendron differs in many respects from that responsible for asthma and allergic rhinitis but is similar to the cutaneous sensitization developing after exposure to other plants and plant extracts, to chemicals and to metals. The differences between these two varieties of allergy have been described in detail in the literature.[33] The characteristic features of dermal sensitization responsible for dermatitis are as follows: No serum antibodies have so far been satisfactorily demonstrated by passive transfers and no protective antibodies [34] similar to those developing after the treatment of hay fever have been described; there is no apparent hereditary predisposition [35] to the acquisition of the sensitivity causing dermatitis venenata; anaphylactic shock with edema and bronchospasm does not occur because the skin is by far the most sensitive tissue and appears to be the chief shock organ. Our meager knowledge about cutaneous sensitization to plants, chemicals and metals has been obtained through clinical and experimental use of the contact or patch test. First used to demonstrate cutaneous sensitivity to mercury by Jadassohn,[36] it was later employed by all chemists to test the toxicity of chemical substances extracted from ivy, sumac and lac plants and saps. More recently this test has been employed by clinicians to determine susceptibility to Toxicodendron, to follow experimental sensitization induced in man and animals and to study variations in sensitivity during oral or parenteral prophylactic therapy.

Infants at birth [37] and with rare exceptions children under 5 years of age [38] give negative reactions to extracts of T. radicans (L). On the other hand, infants have been experimentally sensitized. Strauss [37] sensitized 72.9 per cent of 48, some of whom retained their sensitivity for eighteen to twenty months. He induced sensitization by cutaneous contact combined with ingestion but could not sensitize infants by either the oral or the intramuscular administration of extracts alone.[39] With one or two exceptions, reports indicate that boys and girls of camp age give a higher percentage of positive reactions than adults. Among children in camps,

25. Sweet, E. A., and Grant, C. V.: Pub. Health Rep. **35**: 433, 1920.
26. Dermatitis Venenata, Queries and Minor Notes, J. A. M. A. **102**: 1517 (May 5) 1934.
27. Pfaff.[13] Tschirch and Stevens.[14]
28. Maisch, J. M.: Am. J. Pharm. **38**: 4, 1866.
29. McNair, J. B.: Am. J. Botany **8**: 242, 1921. McNair.[23]
30. von Adelung, E.: An Experimental Study of Poison Oak, Arch. Int. Med. **11**: 148 (Feb.) 1913.
31. McNair, footnotes 29 and 11. Shelmire.[6]
32. Spain, W. C., and Cooke, R. A.: J. Immunol. **13**: 93, 1927.
33. Coca, A. F., and Cooke, R. A.: J. Immunol. **8**: 163, 1923.
34. Loveless, M. H.: J. Immunol. **38**: 25, 1940; South. M. J. **33**: 869, 1940; J. Immunol. **44**: 1, 1942.
35. Coca, A. F.: Specific Diagnosis and Treatment of Allergic Diseases of the Skin, J. A. M. A. **103**: 1275 (Oct. 27) 1934.
36. Jadassohn, J.: Verhandl. d. deutsch. dermat. Gesellsch., 1896, p. 3.
37. Shelmire, B.: Contact Dermatitis from Weeds: Patch Testing with Their Oleoresins, J. A. M. A. **113**: 1085 (Sept. 16) 1939. Strauss.[35]
38. Spain, W. C.: J. Immunol. **7**: 179, 1922. Coca, A. F., ibid. **7**: 193, 1922.
39. Strauss, H. W.: J. Allergy **5**: 568, 1934.

Clarke and Hanna [40] and Simon and Lotspeich [41] obtained respectively 85 and 82.1 per cent of positive reactions. Spain [8] in a small group averaging about 15 years of age found 84 per cent reactive. On the other hand, Molitch and Poliakoff [42] found that only 22.9 per cent of a group of 292 white boys were positive. Either the extracts used for testing this group were not as potent as those employed by the other observers or, since the group tested was presumably from a different social stratum, the groups tested by these different observers represent extreme and not average samples in regard to previous exposure and sensitization. Among adults the percentage of susceptibles as determined by the patch test is remarkably uniform in groups from various parts of the country. Spain [8] in a group predominantly of adults, Spain, Newell and Meeker [43] and Deibert, Menger and Wigglesworth [44] in two separate racial groups of adults obtained 65 per cent, 60 per cent and 58.2 and 56 per cent respectively. Shelmire [45] found that approximately 50 per cent of a group of medical students reacted. While the patch test cannot be employed with certainty to determine whether or not a person is clinically sensitive to casual exposure, the results of the tests are said to parallel the clinical histories fairly accurately.[8] Simon and Lotspeich [41] observed 19 children with negative tests through one summer in camp. Only 2 had dermatitis. From the data given, it is possible that these 2 may have been sensitized by previous testing. Spain tested 13 boys, of whom 11 were reactive. On rigorous exposure, only 1 boy with a weakly positive reaction and the 2 with negative tests escaped ivy dermatitis.

In addition to these observations decreased susceptibility has been found to parallel diminished sensitivity to patch tests brought about by oral hyposensitization. An unquestionable relationship is evident between the frankly positive test and susceptibility to ivy after rigorous exposure. On the other hand the casually exposed person may not succumb even though his test is positive. Shelmire estimates that 25 per cent of the population in the neighborhood of Dallas is clinically sensitive and Zisserman [46] observed that 36.4 per cent of nearly 1,300 adult men whose susceptibility and reactions to tests were not known developed dermatitis on casual exposure in the field. Of known susceptibles, 52.8 per cent had rashes.[46] These incidences are approximately those obtained after prophylactic treatment in some groups of patients mentioned in following paragraphs in whom the skin test was not modified. Apparently, when casually exposed, only about half of a group with positive tests contract dermatitis.

All the chief races appear to be equally susceptible if they have been equally exposed. Deibert, Menger and Wigglesworth [44] obtained almost identical percentages (58.8 and 56 respectively) among adult white subjects and American Indians living west of the Mississippi River. One racial exception so far encountered is the Eskimos on Baffin Island, none of whom reacted to tests with ivy extracts.[47] It is believed that these Eskimos have never been exposed and sensitized. Some adults with negative tests can be sensitized experimentally [48] while others are extremely refractory.[49] Apparently sensitivity may also be lost. Strauss [39] found that some infants whom he had sensitized had lost their artificially acquired sensitization after eighteen to twenty months. Shelmire [45] has also attributed an extremely low proportion of positive tests, 8.5 per cent, among patients averaging 70 years of age in a convalescent home to continuous confinement with resultant lack of exposure.

SENSITIZATION WITH URUSHIOL: EXPERIMENTAL DATA

Experiments with primulin ($C_{14}H_{18}O_3$ or $C_{14}H_{17}O_2OH$) carried out between 1924 and 1930 formed the ground work for similar experiments with ivy. Primulin is the active chemical substance causing dermatitis from contact with Primula obconica. Both man and animals have been sensitized with extracts and the isolated active principle.[50] In 1934 Rackemann and Simon [51] and the Simons and Rackemann [52] reported that the skin of guinea pigs could be sensitized by treating it with extracts of Toxicodendron. Sensitization did not follow intraperitoneal, intramuscular or subcutaneous inoculations. Simon [53] found that, if an area of skin was treated with extract and then excised within twenty-four hours, the sensitizing antigen had already been distributed and the skin of the animal would become uniformly sensitive. No tissues other than the skin appeared to be sensitized. Landsteiner and Jacobs [54] sensitized guinea pigs with urushiol. They confirmed the observation that application of the antigen to the skin was surprisingly superior to any other method of sensitization and demonstrated cross sensitization with urushiol and ivy extracts. Because people sensitive to ivy are equally sensitive to oak and sumac, some observers have assumed that the active substances in all these plants are identical.[55] Spain, Newell and Meeker [43] tested adults with extracts of ivy and oak (T. radicans [L] and T. toxicodendron [L]). From their data, consisting of series of tests on many subjects with dilutions of extracts, they concluded that people who were sensitive to ivy and oak varied in degree of sensitivity to the concentrations of extract used in a definitely mathematical manner. When curves of the varying degrees of sensitivity were plotted against the percentages of positives, the curves for ivy and oak were practically superimposed. However, these data obtained from patch tests can be considered only contributory evidence to the possibility that the irritants from oak, ivy and sumac are identical, just as the occurrence of similar polyphenolases in the saps of these plants suggests that the substrates are chemically similar but are not necessarily the same.

40. Clarke, J. R., and Hanna, C. M.: J. Allergy **13**: 599, 1942.
41. Simon, F. A., and Lotspeich, E.: J. Invest. Dermat. **2**: 143, 1937.
42. Molitch, M., and Poliakoff, S.: Prevention of Dermatitis Venenata Due to Poison Ivy in Children, Arch. Dermat. & Syph. **36**: 1086 (Nov.) 1937.
43. Spain, W. C.; Newell, J. M., and Meeker, M. G.: J. Allergy **5**: 571, 1934.
44. Deibert, O.; Menger, E. F., and Wigglesworth, A. M.: J. Immunol. **8**: 287, 1928.
45. Shelmire, B.: South. M. J. **4**: 337, 1940.
46. Zisserman, L.: J. Allergy **12**: 474, 1941.
47. Heinbecker, P.: J. Immunol. **15**: 365, 1928.
48. Field, H., and Sulzberger, M. B.: J. Allergy **7**: 139, 1936. Shelmire.[37]
49. Simon and Lotspeich.[41] Shelmire.[37]
50. Low, R. C.: Anaphylaxis and Sensitization, New York, William Wood & Company, 1924. Bloch, B., and Steiner-Wourlish, A.: Arch. f. Dermat. u. Syph. **152**: 283, 1926. Bloch, B.: Role of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**: 175 (Feb.) 1929. Bloch, B., and Steiner-Wourlish, A.: Arch. f. Dermat. u. Syph. **162**: 349, 1930.
51. Rackemann, F. M., and Simon, F. A.: Science **79**: 344, 1934.
52. Simon, F. A.; Simon, M. G., and Rackemann, F. M.: J. Immunol. **27**: 113, 1934.
53. Simon, F. A.: J. Immunol. **30**: 275, 1936.
54. Landsteiner, K., and Jacobs, J.: J. Exper. Med. **64**: 625, 1936.
55. Strauss, H. W.: J. Allergy **2**: 137, 1931; footnote 39.

Although Landsteiner and Jacobs observed cross reactions between urushiol and ivy extracts, they obtained cross reactions with other catechols, such as geranyl and 4 tetradecylcatechol, as well. These catechols have side chains similar to but not identical with the side chain of urushiol. Apparently too much reliance should not be placed on skin tests or immunologic evidence alone as a means of establishing chemical identity.

THE EVOLUTION OF PROPHYLACTIC AND PHYLACTIC IVY TREATMENT BY THE ENTERAL AND PARENTERAL ADMINISTRATION OF EXTRACTS

Chewing ivy leaves to prevent dermatitis has been a folk treatment in this country for generations. Although this practice supposedly was common among the Indians, it does not appear to have been a universal custom.[56] Some practitioners[57] have advocated this preventive measure even in recent years.[58] In 1917 Schamberg,[59] who popularized oral prevention and treatment, stated that the ingestion of increasing doses of alcoholic ivy extract would prevent and cure the dermatitis. He maintained that no necessity for injections existed, because oral therapy was sufficiently satisfactory.[10] But Strickler[2] advocated the combined method of treatment, that is, the oral and parenteral administration of dilutions of the alcoholic extract in increasing doses, and this soon became the method of choice. Between 1921 and 1927 Spain and Cooke[32] treated patients with alcoholic extracts orally, by injection and some by the combined method. During the course of the study the extraction of the material used was modified to some extent. Extracts of the fresh leaf in alcohol deteriorated possibly because of the water in the final extract,[8] so the leaves were then dried and extracted in absolute alcohol.[32] From subsequent studies[43] it would appear that extracts prepared by them must be fairly uniform. The injection of alcoholic extracts proved to be painful, so the extract was diluted with salt solution just before it was injected. In 1925 Clock[60] suggested almond oil as a diluent. Most commercial preparations have been diluted in oil since that time, but the oils employed have varied. Acetone and ether[61] have also been introduced as extractives of the fresh leaf. The ether extracts in oil and in pills and capsules have been used for oral and parenteral treatment. It is believed by some that acetone and ether are superior extractives.[62] This may be true for the fresh leaf because of the differing solubilities and activity of laccase in varying concentrations of acetone, alcohol and ether. With leaves rapidly dried at low temperatures these solvents should be equally satisfactory, because urushiol is readily soluble in all. Conclusions in the earlier literature regarding the comparative value of these extracts for treatment and for proyhylaxis as well as the comparative value of oral and of parenteral therapy are difficult to evaluate, because prevention and treatment of the acute dermatitis were frequently confused and Strickler's combined method of administration was most commonly employed. In recent years several concrete questions have arisen concerning the use of these extracts. First, as determined by patch tests, can the sensitivity of the skin be sufficiently modified to account for some of the excellent prophylactic results reported in the past following oral or intramuscular therapy? Second, even though the test does not show lessened sensitivity after therapy, is the clinical evidence pointing to greater resistance to dermatitis satisfactory and sufficient to justify the use of the extracts? Third, should extracts be used in the treatment of the acute dermatitis?

THE EFFECT OF THE ADMINISTRATION OF IVY EXTRACTS ON THE CUTANEOUS TEST

In 1925 Krause and Weidman[63] studied the effect of Strickler's combined injection and oral method on the skin sensitivity of 7 susceptible persons. Ten days after the course was finished, application of the extracts to the arms gave severe reactions. The extracts used were potent, because most of these subjects developed perianal dermatitis and the extracts had been used for testing. In 1927 Spain and Cooke[32] reported that sensitivity to the test was unchanged after protracted series of injections of alcoholic extracts. Blank and Coca, convinced by previous experiments that tests were unmodified by prophylactic inoculations, omitted testing both control and inoculated groups in their study of preventive therapy. In 1939 Simon and Lotspeich[41] observed that inoculations with acetone extracts failed to decrease the dermal sensitivity of 8 patients. According to Greenberg and Mallozzi,[64] no convincing variations in skin sensitivity were obtained in a control series and in one composed of patients inoculated with acetone extracts in oil (one or two inoculations). In these previous experiments, with the possible exception of those of Blank and Coca and of Greenberg and Mallozzi, who used measured quantities of acetone extracted solids in oil, standardization of the doses of extract given were based only on the proportion of leaf to the solvent and the potency of the dilutions on skin testing. The exact amount of active extracted urushiol was not determined. Recently Shelmire[6] tried oral therapy with ether extracts of both fresh and slowly dried leaves. He believed that the extracts from the fresh leaves were five to ten times more potent. The ether was evaporated and the solid residue was diluted 1 to 10, 1 to 25 and 1 to 50 in corn oil. These dilutions were given in increasing doses over several months. He found that the skin sensitivity to tests was definitely diminished in 20 patients who ingested from 1 to 3 cc. of the ether extractable residue in the course of seven or eight months.[65] Gold and Masucci[66] likewise have used ether extractable residue in pills. Twenty patients with positive reactions were given increasing doses of ether extracted residue increasing from 0.5 to 15 mg. daily over a period of forty-five days. Seventeen of these showed diminished reactions after the course was finished. When the patients with lessened sensitivity

56. Gilmore, M. R.: Uses of Plants by Indians, in Thirty-Third Annual Report, Department of Agriculture, Entomology and Plant Quarantine Bureau, 1911-1912, p. 100.
57. Dakin, R.: Am. J. M. Sc. **4**: 98, 1829.
58. Alumbaugh, W. E.: M. World **16**: 298, 1898. Duncan, C. H.: New York M. J. **104**: 901, 1916. Cooper, H. M.: M. J. & Rec. **136**: 297, 1932.
59. Schamberg, J. F., in discussion on papers of Hermann, Knowles and White, J. A. M. A. **68**: 87 (Jan. 13) 1917.
60. Clock, R. O.: Ann. Clin. Med. **4**: 519, 1926; footnote 76.
61. Caulfeild, A. H. W.: Canad. M. A. J. **37**: 18, 1937; footnotes 84 and 85.
62. Howell, J. B.: Solubility of Dermatitis-Producing Fraction of Poison Ivy, Arch. Dermat. & Syph. **44**: 665 (Oct.) 1941. Shelmire, footnotes 6 and 65.
63. Krause, G. L., and Weidman, F. D.: Ivy Poisoning: Preventive Treatment, with Especial Reference to Element of Individual Sensitivity, J. A. M. A. **84**: 1996 (June 27) 1925.
64. Greenberg, S., and Mallozzi, E. D.: Experiments in Poison Ivy Sensitivity, Arch. Dermat. & Syph. **42**: 290 (Aug.) 1940.
65. Shelmire, B.: Hyposensitization to Poison Ivy, Arch. Dermat. & Syph. **44**: 983 (Dec.) 1941.
66. Gold and Masucci, footnotes 88 and 89.

were tested ten months later, 5 had returned to the original level of sensitivity, 5 showed no change, and the rest showed slight or definite increases. These patients ingested between 2.9 and 3.7 Gm. of residue during "immunization." Apparently if the doses of residue given orally are sufficiently large the test sensitivity as well as the clinical susceptibility are diminished and parallel each other. In the last experiment mentioned, rigid field controls in which a control group with positive tests all were found susceptible, 10 of the "immunized" group were completely and 6 partly protected. Protection occurring clinically as the result of injections when the skin sensitivity has not been modified has not been explained. It is possible that the test as it is used will not detect minor degrees of hyposensitization sufficient to protect mildly sensitive people to slight and casual contacts. Until this discrepancy is satisfactorily explained, some doubt must linger in the minds of critical therapeutists concerning the real value of preventive parenteral therapy with ivy extracts.

PROPHYLACTIC INOCULATION WITH IVY EXTRACTS: CLINICAL DATA

Most of the literature previous to 1925 on clinical results obtained with ivy extracts is difficult to evaluate. Strickler's method was most commonly employed. He believed the active substance was a glucoside and followed the procedure of Syme [67] in extracting with alcohol. Schamberg, who had first aroused interest in the ivy problem, advised oral prophylaxis but later advocated phylactic treatment as well. Strickler gave his patients alcoholic extracts orally and by injection, a method which Schamberg [10] never endorsed. The prevalent procedure at that time seems to have been to treat the patient during the acute stages of the dermatitis by injections and to continue oral therapy for prophylaxis, but some treated patients phylactically both by injection and by mouth. The word "treatment" was used loosely and might imply remedial measures either for prevention or for cure. Unfortunately, although some of the authors referred only to prevention and some only to treatment of the acute rash, their publications have been quoted as references for either phylactic or prophylactic therapy, the distinction originally drawn having been lost. In 1919 Schamberg [68] advocated immunization with tincture, beginning with small doses daily and increasing up to a uniform dose, which was continued daily throughout the summer. Strickler apparently treated the acute dermatitis by injections and followed with orally given tincture for prophylaxis.[69] Later he advised this combined mode of therapy as a preventive.[70] Alderson and Pruett [71] and Bivings [4] reported satisfactory protection using this method. On the other hand, when Krause and Weidman [63] found that the injections and the oral tincture failed to modify the intensity of patch tests with ivy extracts, they doubted the efficacy of the procedure. None of the clinical reports had control data. Furthermore, it appears that the remarks and articles [72] of some authors commenting favorably on treatment have since been construed as favorable to prophylactic therapy.

Previous to 1925 most authors stressed treatment, but subsequently the reports have been concerned chiefly with prevention and only occasional investigators have advocated phylactic injections. Spain and Cooke [32] reported a series of cases in 1927 treated prophylactically with injections of alcoholic extracts diluted with salt solution. Beginning about April with the weakest dilution which gave a satisfactory skin test, they gradually increased the size of the doses and continued at weekly intervals through the summer with a standard dose of the strongest tolerated dilution. Although the reactions to patch tests were not diminished in intensity following ordinary exposure to ivy such as occurred in everyday life, according to collected reports 59 per cent of 98 patients were symptom free and 37 per cent improved over previous years. Subsequent to this report several investigators have studied groups of patients inoculated prophylactically according to this procedure with similar alcoholic extracts. In 1936 Molitch and Poliakoff [73] gave 40 boys nine to twenty weekly injections. All of these boys were sensitive to patch tests with ivy but none who were inoculated had a rash. In a skin sensitive control group 9 of 14 contracted dermatitis. In midsummer the following year the same investigators [42] gave similar courses of injections to 42 boys who had suffered from dermatitis in the preceding ten weeks. In the treated group only 1 had dermatitis subsequently, in contrast to 8 controls all of whom were afflicted. In 1938 Biederman [74] selected 30 subjects who had had ivy or oak dermatitis in the two preceding summers. Thirteen were given ivy extracts and 13 oak extracts according to the procedure of Spain and Cooke except that inoculations were begun in January. Inoculations were given at weekly intervals for six weeks and then continued monthly through the summer. Only 4 of the 26 subjects inoculated contracted rashes, but all of a small control group (4) had dermatitis on exposure. Clarke and Hanna [40] followed 82 boys, 86 per cent of whom were positive to tests, after giving five injections of alcoholic extract previous to departure for camp. Of 35 who had had dermatitis previously 16 escaped, while the others had some dermatitis, 7 as severely as before. Of the 47 inoculated subjects remaining, none of whom had had ivy rashes before, 7 had mild eruptions. Protection in this group was better among the boys who had never had ivy dermatitis. Among those with ivy rashes in preceding summers the five preseasonal injections given appear not to have protected as well as courses of inoculations continued through the season.[75] There appears to be no unfavorable report on this method of prophylactic therapy. The favorable evidence, however, is all clinical, the exposure to ivy was usually casual, and the skin test sensitivity was not modified. If recent experimental evidence is correct, subjects in whom the skin sensitivity is not diminished by prophylactic therapy will not withstand rigorous controlled exposure.

67. Syme, W. A.: Some Constituents of the Poison Ivy Plant, Dissert., Baltimore, Johns Hopkins University, 1906.
68. Schamberg, J. F.: Desensitization of Persons Against Poison Ivy, J. A. M. A. **73:** 1213 (Oct. 18) 1919.
69. Strickler, A.: J. Cutan. Dis. **36:** 327, 1918.
70. Strickler, A.: Toxin (Antigen) of Rhus Toxicodendron and Rhus Venenata in Treatment and Desensitization of Patients with Dermatitis Venenata, J. A. M. A. **80:** 1588 (June 2) 1923.
71. Alderson, H. E., and Pruett, H. J.: California State J. Med. **19:** 188, 1921.

72. Cole, H. N.: Poison Ivy Treatment, Arch. Dermat. & Syph. **11:** 265 (Feb.) 1924. Wise, F.: Poison Ivy Treatment, ibid. **11:** 266 (Feb.) 1925. Donald.[95] Alderson.[9] Williams.[5] Williams and MacGregor.[5]
73. Molitch, M., and Poliakoff, S.: Prevention of Dermatitis Venenata Due to Poison Ivy in Children, Arch. Dermat. & Syph. **33:** 725 (April) 1936.
74. Biederman, J. B.: New England J. Med. **219:** 117, 1938.
75. Molitch and Poliakoff.[42] Biederman.[74]

Injections with alcoholic extracts are painful even when salt solution is used as a diluent. Clock [76] suggested that oil be used instead of saline solution. Subsequently alcoholic extracts [77] and extracts in acetone [78] and with ether [79] were diluted with oil and used parenterally and orally in attempts to establish protection. Since absorption from oil is delayed, larger doses of extract could be given in one inoculation, so the customary course of ten to fifteen injections was shortened to a few, each dose containing correspondingly greater amounts of concentrated extract. In recent years the tendency has grown to measure the dose in cubic centimeters or milligrams of solid substance obtained by the evaporation of the extracting solvent from the concentrated extract. There is no evidence to suggest that the oily material procured in this way approaches the purity of urushiol. Gowen [80] prepared an alcoholic extract in almond oil similar to that with which Clock [81] had obtained favorable protective results. He believed that 5 of 8 patients given one or two inoculations were protected for one or two years. In 1936 Blank and Coca [82] criticized all previous reports on preventive therapy because no control groups were included with the data. They divided a number of men in a camp in three groups. One group was given four weekly injections of oil containing in all 2 mg. of solids extracted from ivy leaves with acetone, a second group 26.4 mg. of solids, while the third was used as a control. The groups were intermingled while at work. In these groups the incidence of dermatitis was 20, 7 and 66.7 per cent respectively. Bachman [83] selected 14 children, to whom he gave two injections each containing 6.6 mg. of acetone extracted solids. All had had rashes previously. Of 13 who were exposed, 85.7 per cent were unprotected and, although an additional 6.6 mg. was given, 7, or 57 per cent, of these were still susceptible.

In 1937 and 1938 Caulfeild [84] reported that he had injected solutions in oil of solids obtained by evaporating ether extracts of ivy. The method was similar to that previously employed in making extracts of tulip bulbs for the treatment of tulip fingers.[85] The solids were diluted by volume, but the amount of solids given each patient cannot be calculated from the data given. From a small group of patients without controls, he concluded that recurrences were prevented and the skin sensitivity was diminished in intensity. More recently Gold [86] encountered complete failure to protect with ether extracts injected prophylactically through one summer. Shelmire [65] has concluded from his experience that intramuscular injections are of no prophylactic value, sometimes because the material injected is not potent but chiefly because the total amount of solids injected is too small either to modify the skin test or to reduce susceptibility on clinical exposure. All the literature so far suggests the possibility that, whether the administration of extracts is oral or parenteral, the doses must be sufficiently large to cause a series of mild dermal reactions if the skin test is to be modified or the patient protected against rigorous exposure.

76. Clock, R. O.: M. J. & Rec. (supp.) **93**: 122, 1925.
77. Clock.[80] Gowen.[80]
78. Blank and Coca.[82] Greenberg and Malozzi.[64] Bachman.[83]
79. Zisserman, L., and Birch, L.: J. Allergy **10**: 596, 1939. Caulfeild, footnotes 84 and 61, first reference. Shelmire.[65]
80. Gowen, G. H.: J. Allergy **4**: 519, 1933.
81. Clock, footnotes 60 and 76.
82. Blank, J. M., and Coca, A. F.: J. Allergy **7**: 552, 1936.
83. Bachman, L. C.: J. Pediat. **12**: 31, 1938.
84. Caulfeild, A. H. W.: J. Allergy **9**: 535, 1938; footnote 61, first reference.
85. Caulfeild, A. H. W.: Canad. M. A. J. **34**: 506, 1936; J. Allergy **9**: 535, 1938.
86. Gold, H.: J. Allergy **13**: 605, 1942.

RECENT ORAL PROPHYLACTIC TREATMENT WITH IVY EXTRACTS

Galenic tinctures and alcoholic extracts are administered commonly for oral prophylactic therapy. Although stable triturates from alcoholic extracts were prepared as early as 1927,[32] it was believed that patients would forget to take oral preparations and the course required to establish "immunity" was too long in comparison to the time necessary for a similarly effective course of injections. Using the ether extractable solids diluted in corn oil enterally Shelmire [87] was able to reduce skin sensitivity to ivy extracts. From 1 to 3 cc. of the solids diluted and given in increasing daily doses were ingested in the course of several months. Zisserman [46] administered enteric coated capsules, each containing 0.01 mg. of ether extracted solids to 100 men; 0.01 mg. was given daily for seven days, then weekly until each subject had taken from 0.15 to 0.30 mg. Of this group 32 per cent contracted dermatitis on normal field exposure, as compared to an incidence of 36.4 per cent among a very large control group similarly exposed. The protection afforded by this prophylaxis was considered nihil. In the following year, 1942, Gold and Masucci [88] selected 20 subjects for oral prophylaxis with a control group of 8, all with positive skin tests. Beginning with 0.5 mg. of ether extracted solids daily in pills, they increased the daily dose to 150 mg. in the course of forty-five days. Ten of the group of 20 were completely protected, 6 partially and 4 not at all. By the end of the course, each of the 20 people had ingested between 2,900 and 3,700 mg. of solids. The control group was 100 per cent susceptible. In a subsequent statement [89] additional data on 13 more men were submitted. In the first group studied toxic rashes were observed in 80 per cent in the first three or four weeks of therapy when the daily dose was being increased. In the second group the dose given daily was increased more slowly in the early part of the course and the whole period of ingestion was extended to two months. Ten of this group developed toxic rashes during the first few weeks, even with this added precaution. Although these investigators proved that complete protection could be established in about half dermal sensitive subjects and some others partly protected, and that the skin sensitivity could be reduced in intensity by oral administration of ivy extracts, the method was not considered safe or practical because of the high percentage of reactions. They thought these toxic reactions might be avoided if the course was made still longer and the doses increased more gradually. However, on retesting several of the group a few months after the courses were completed they discovered that the sensitivity in some had reverted to the former levels and so questioned the advisability of an extensive course to obtain such temporary hyposensitization.

EXPERIMENTAL APPROACH TO IVY IMMUNIZATION

In the preceding sections, suggestions and conclusions have been based on factual data found in the reports of the various investigators cited. Possibilities still open for

87. Shelmire, footnotes 37 and 65.
88. Gold, H., and Masucci, P.: J. Allergy **13**: 157, 1942.
89. Gold, H., and Masucci, P.: J. Allergy **13**: 606, 1942.

experimental approach so far not satisfactorily covered in the literature were not discussed. Two methods for ivy prophylaxis—the oral and the parenteral administration of extracts—have been studied extensively. Recent studies, where small oral doses were given, showed no effect on the resistance of the patients to ivy dermatitis, but large doses given on a graduated ascending scale both modified or reversed the positive skin test and temporarily protected many of the patients against rigorous exposure to ivy. Severe reactions were encountered when the course was short but these were less severe when the same amount of solid oleoresin was given orally during the course of several months. In fact, although occurring, the reactions were said to be negligible with the longer period of administration. Since no careful statistical study of the perennial method of oral administration is available in the literature, this experimental study should be attempted. None of these more potent products have been marketed and none have been submitted to the consideration of the Council. The tinctures so commonly used are unstandardized and according to the literature of questionable and variable potency.

Extracts for parenteral administration have been marketed and several brands have been accepted by the Council. Hitherto, these have been unstandardized. Available published statistical evidence suggests that these parenteral inoculations, with carefully prepared and potent extracts intelligently given, protect the patient to some extent against casual or clinical exposure, even though the skin test sensitivity is not apparently modified. So far no extensive study of prophylaxis by perennial inoculations is available. Since this method appears to be the most satisfactory procedure for pollen prophylaxis, it should be tried for ivy. Shelmire found that even though the positive skin test was not completely reversed, varying degrees of hyposensitization to the test afforded some protection to clinical or casual exposure to ivy. The sensitivity of patients given preseasonal and perennial prophylactic injections should be studied further. Differences in sensitivity before and after prophylaxis might be detected if the patients were tested with a single dilution applied to the skin for varying periods of time. Testing has previously been done with several dilutions of varying strength. The duration of the application may be important. So far the literature suggests that when the skin test has been modified by oral prophylaxis, the patient has been desensitized. The possibility that an immune reaction similar to that occurring after pollen inoculations may also occur after inoculations with ivy has not been investigated.

REACTIONS FOLLOWING THE ADMINISTRATION OF IVY EXTRACTS

Reactions have frequently been reported in the literature both from oral and from parenteral administration of ivy extracts. With extracts given by mouth, perianal dermatitis has been the commonest complication. It was reported by Dakin [57] over a hundred years ago in patients who had chewed fresh ivy leaves. Warren [90] tried taking the tincture himself in 1919 but developed severe pruritus ani. Although the mucous membranes according to most observers have appeared insensitive to ivy and ivy extracts, stomatitis has been observed along with perianal rash after fresh leaves were chewed.[91] Whether the mucous membranes are actually sensitive to strong solutions of ivy extract or whether the stomatitis sometimes observed results from an escharotic action of urushiol cannot be decided from reports and experiments made so far. It is believed by some [92] that urushiol and strong concentrations of ivy extracts are primarily irritating when applied to the skin of man and animals. Simple polyphenols, although they darken the skin, lack this effect.[12]

The gastrointestinal tract is irritated by the ingestion of ivy extracts. According to Gold and Masucci, many of the group whom they treated orally suffered from abdominal symptoms during the first few weeks of therapy but became tolerant as the doses were increased. Occasionally, when proper precautions have not been observed during oral therapy, the mucous membranes of the mouth and esophagus have sloughed following the ingestion of strong solutions. Toxic rashes occurred in almost all of the group studied by Gold and Masucci [88] and have been observed by Shelmire [6] following large oral doses of ether extracts. When intramuscular therapy was first used, several physicians reported rashes following injections. The tender skin of the ankles and wrists was most commonly affected, but generalized pruritus was reported. Spain and Cooke [32] observed that when the parenteral doses were increased in size too rapidly the sites of old ivy tests might flare up and rashes might occur even though the site of the inoculation was neither tender nor swollen. Although ordinarily when alcoholic extracts were used a certain amount of momentary pain was experienced, there was no prolonged inflammatory reaction at the site. With the introduction of larger doses of ivy extract in oily vehicles for intramuscular therapy, intense pain, swelling and edema have been encountered in some patients, especially in those treated phylactically. Since the absorption of the larger dose is delayed by the nature of the vehicle, the reaction—swelling and inflammation—may continue over several days. Since ivy dermatitis is obviously a sensitization phenomenon, local, focal and general reactions should be anticipated after the injection of large doses of ivy extract in very sensitive patients. While solutions of extracts in oil permit the administration of relatively larger doses because absorption is delayed, in sensitive subjects absorption of this larger dose often causes severe incapacitating local reactions. One well established principle in the therapy of diseases resulting from sensitization is that the symptoms and clinical characteristics of the disease can often be reproduced by inoculation with certain doses of the antigen. This dose varies in different patients according to their degree of sensitivity. Accordingly, treatment of the acute symptoms by injections of antigen is against all accepted scientific and therapeutic principles unless the patient has previously been well immunized and small doses, well within the tolerance of the patient, are given to maintain immunity through a long season of exposure. Severe local reactions and exaggeration of symptoms are signs of dangerous overdosage. In this connection Corson's observations on Strickler's method of phylactic therapy are interesting. He found that many times when he employed oral and parenteral

90. Warren, L. E.: Desensitization of Persons Against Ivy Poisoning, Correspondence, J. A. M. A. **73**: 1382 (Nov. 1) 1919.

91. Silvers, S. H.: Stomatitis Venenata and Dermatitis of Anal Orifice from Chewing Poison Ivy Leaves (Rhus Toxicodendron), J. A. M. A. **116**: 2257 (May 17) 1941.

92. Toyama.[12] Simon.[52] Landsteiner and Jacobs.[54]

therapy for acute dermatitis the rash was intensified. Unfortunately, as most extracts are now supplied commercially, there is but one dose, which is intended for either prophylaxis or treatment and is given without regard to the level of sensitivity of the individual to whom it is administered. Furthermore, no opportunity is commonly afforded to give serial doses of increasing strength, which are essential in the proper "immunization" or "desensitization" of the sensitive patient.

PHYLACTIC TREATMENT WITH IVY EXTRACTS

When phylactic treatment was first popularized, the clinical results were considered brilliant.[93] There were, however, a few contradictory reports.[94] Although some of these authors who reported extensive series of patients treated for acute lesions had a few failures, nearly all who were treated were considered improved clinically. The itching seemed to subside and the course was believed shortened. These were only clinical impressions, and no data were offered to show that, in comparison with untreated patients, the course of the disease was actually modified. In 1925 Donald [95] offered some statistical data, not on the duration of the disease but on the length of time required for treatment among groups of patients who were given ivy extracts and those who were not. In the infirmary of the University of California 638 students were seen for ivy dermatitis within twenty-two months. The average number of days of treatment of all kinds, either with or without ivy extracts, in this group was 3.1 days. Severe dermatitis was treated by oral, parenteral or combined therapy. The average time of treatment in this group was 2.9 days. Donald states further that the average duration of treatment among those not given this therapy was four days. According to McNair,[96] the average number of days of hospitalization of 76 patients for ivy dermatitis previous to 1921 was three days in this same infirmary. These figures are offered for comparison. The differences are inconsiderable. In more recent literature, prophylaxis and not phylactic therapy has been stressed, although occasional favorable reports have appeared [97] within the last decade. No further statistical evidence has been offered in these later reports that the course of the disease has been shortened or modified. In 1938 Sompayrac [98] studied the effect of alcoholic extracts given intramuscularly on the duration and symptomatic course of local dermatitis induced by patch test. Nine of twenty-three skin sensitive subjects were given three or four injections in the course of two days after a local skin reaction has been induced. The course of the induced reaction was not modified, nor did it differ in any respect from the course of the local rash induced in 14 control subjects. The injected sites were painful and swollen. In 1 subject generalized pruritus followed an inoculation. The data offered in the literature are not convincing in regard to the phylactic value of treatment with antigens of ivy orally or parenterally. Ivy dermatitis is a self-limited disease of short but indefinite duration with variable symptoms, and no satisfactory evidence has been brought forth to show that the course has been changed for the better by this therapy. Since it is known that many patients are made worse because severe reactions occur when large doses of extracted solids are injected and since the practice is not in conformity with theory, it is believed that the treatment of acute ivy rashes either parenterally or orally with ivy extracts should be vigorously discouraged.

93. Ormsby, O.: Poison Ivy Treatment, Arch. Dermat. & Syph. **11:** 266 (Feb.) 1925. Schamberg.[10] Strickler, footnotes 2, 5 and 70. Alderson.[3] Alderson and Pruett.[71] Bivings.[4] Williams.[5] Williams and MacGregor.[5] Cole.[73] Donald.[95] Wise.[72]

94. Corson, E. F.: The Value of the Toxin of Rhus Toxicodendron and Rhus Venenata, Correspondence, J. A. M. A. **81:** 59 (July 7) 1923. Templeton, H. J.: Untoward Reactions Following Toxin Treatment for Dermatitis Venenata, Arch. Dermat. & Syph. **20:** 83 (July) 1929. Morrow.[9] Warren.[90]

95. Donald, W. G.: California & West. Med. **23:** 8, 1925.

96. McNair, J. B.: Pathology of Rhus Dermatitis, Arch. Dermat. & Syph. **3:** 383 (April, pt. 1) 1921. McNair.[11]

97. Gay, L. N.: J. Allergy **13:** 609, 1942. Sharlit, H., and Newman, B. A.: New York State J. Med. **37:** 61, 1937. Caulfeild, first references in footnotes 61 and 84. Gowen.[80]

98. Sompayrac, L. M.: Am. J. M. Sc. **195:** 361, 1938.

SUMMARY AND CONCLUSIONS

Although more than fifty species of poison ivy, oak or vine have been described as native to North America, only three, classified as Toxicodendron, are described by conservative botanists and accepted by the U. S. Herbarium in Washington. According to some observers, these species might be considered subvarieties of a single species which has been modified by climatic and geographic environment. Poison or swamp sumac has also been included in this classification as a species of Toxicodendron. The poisonous substance in at least one species of ivy has been chemically identified as urushiol, the active factor in the sap of the lac trees of Japan, China and Indo-China, and the chemical properties of the dermallergens isolated from the other species of ivy or oak and from swamp sumac are such that it is highly probable that urushiol is the irritant common to ivy, sumac and the lac trees. Immunologic evidence supports this view, so it is believed that a single extract can be used in any attempted prophylactic therapy for the dermatitis caused by any one of these plants. Urushiol is readily oxidized and precipitates in the presence of laccase, a polyphenolase occurring in the saps of all these plants, but is apparently quite stable in slightly acid solution once it has been fractionally separated from this enzyme. Ether is probaby the most satisfactory extractive because it readily dissolves urushiol but not the enzyme. Since laccase is activated as soon as the leaves and twigs of the plants are injured and exposed to air, before extraction the leaves should be dried quickly to prevent oxidation with resulting detoxification of the urushiol. Probably the only satisfactory method of drying to prevent partial oxidation would be to freeze the fresh leaves with solidified carbon dioxide and extract the water in vacuo while the leaves are still frozen.

All observers believe that the typical dermatitis is the result of contact after previous exposure and sensitization to the active substance in the plants. Infants, adults and certain animals have been sensitized with the plant extracts or with urushiol. There is also some evidence that this sensitization resulting from either experimental or natural contact diminishes in intensity if not maintained by repeated exposure.

Persons who show strongly positive skin tests with ivy extracts and are susceptible to the dermatitis can be rendered dermally insensitive to the test and also resistant to rigorous exposure to the plants by the daily ingestion of large increasing doses of ivy extracts. All the evidence suggests that these subjects are desensitized rather than immunized, but unfortunately most are only temporarily "resistant" or "protected" against ivy. If the period of ingestion is short, that is six weeks or less, the doses of extract required to accomplish "desensitization" are so large that rashes and gastrointestinal symptoms have occurred in almost all experimental subjects. These reactions are said to be

negligible when the same amount of extract is administered in smaller doses over a period of seven or eight months. So far, none of these potent extracts for oral therapy have been marketed or submitted to the Council for consideration. There is no satisfactory evidence that the skin test or resistance against ivy on rigorous exposure has ever been modified except by the aforementioned procedure, a procedure which its instigators imply is possibly unsafe except under experienced supervision and probably not worth while because the resistance seems but temporary. There is clinical evidence supported by statistics that intramuscular inoculations have conferred resistance on susceptible persons. The inoculations were begun well before the ivy season and the dose was increased at weekly intervals. But the subsequent exposure was casual in most instances and the sensitivity to the patch test was not modified. While this clinical evidence cannot be disregarded, the fact that the skin test has not been modified and the inoculated subjects have not been rigorously exposed under supervision casts some doubt on the validity of the evidence purporting to show protection afforded by intramuscular inoculation. Since there is no controlled statistical evidence that the daily ingestion of small amounts of extract over a long period will modify the dermal test or give protection and the ingestion of large doses within a period of a few months is still experimental, the method of choice, if one must "immunize" against ivy, appears to be by inoculation with repeated doses of extract begun well before the season and increased in strength at frequent intervals within the tolerance of the patient. This appears to be the method of choice, not because it is believed that the experimental evidence is entirely satisfactory, but because the favorable statistical evidence outweighs the unfavorable, and the objections and queries raised may be satisfactorily explained by subsequent observations.

So far no accepted method of standardization of ivy extracts has been evolved. Since urushiol is a mixture of several components of varying saturation and possibly differing toxicity and there is no evidence that a uniform product has yet been obtained by the different methods of extraction employed, standardization by weight of leaf or by volume or weight of extracted solids can be only an approximation. In experienced hands, extracts of considerable uniformity can apparently be obtained, because different extracts prepared by the same method have given approximately the same percentages of positive skin reactions in similar groups of people. By testing an individual prior to immunization with varying dilutions of such an extract, the strength of the initial dose can be made to conform with the sensitivity of the individual. With commercial extracts, since such adaptation to the individual is scarcely feasible, the initial dose of a standard series should be one adapted to the most sensitive individuals in the population. If the weakest dilution of a preparation which will give a satisfactory skin response in 50 to 60 per cent of an average sample of the exposed adult population is accepted as a standard and inoculations are started with a five or ten fold dilution of this standard solution, this requirement should be satisfied. The series of doses used for "immunization" should be prepared so that the practitioner may have sufficient latitude to meet the requirements of the individual patient. The treatment of the acute rash with ivy extracts should be discouraged, because many patients are made worse and there is no satisfactory evidence that any are helped.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its actions will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

SYRUP OF AMMONIUM MANDELATE.—A syrup containing approximately 40 Gm. of mandelic acid and approximately 4.5 Gm. of ammonia per hundred cubic centimeters. It contains ammoniated glycyrrhizin, anethol or menthol and other flavoring agents and is sweetened with sugar and saccharin.

Actions and Uses.—Ammonium mandelate is used to provide mandelic acid therapy without concurrent use of ammonium chloride as a urine acidifier. In some cases supplementary therapy with ammonium chloride is necessary.

Dosage.—The daily dose for adults should provide 12 Gm. of mandelic acid, administered in divided doses.

Tests and Standards.—

Syrup of ammonium mandelate occurs as a dark brown viscous liquid, possessing a characteristic odor and a bitter taste, with a sweet, licorice-like after-taste. The *pH* of syrup of ammonium mandelate is not below 5.0 nor above 7.0; the specific gravity is between 1.2 and 1.4.

Transfer 2 cc. of syrup of ammonium mandelate to a separator; add 5 cc. of water, 5 cc. of diluted sulfuric acid, and extract the mixture with 25 cc. of ether, filter the ether solution through a cotton plug and evaporate the ether in a stream of warm air: the melting point of the residue is from 118 to 120 C. and it responds to the tests of identity for mandelic acid-U. S. P. Warm 2 cc. of syrup of ammonium mandelate with 5 cc. of sodium hydroxide solution: a strong odor of ammonia is evolved. Ash 1 Gm. of syrup of ammonium mandelate: the residue found is not more than 0.1 per cent.

Transfer an accurately weighed portion of syrup of ammonium mandelate, equivalent to about 20 cc. of the syrup, to a 500 cc. calibrated flask, dilute to the mark with water and mix thoroughly.

Transfer 25 cc., accurately measured, of the prepared solution to an automatic extractor (liquid-liquid), acidify with 5 cc. of diluted sulfuric acid and extract with ether for four hours. When the extraction is complete, evaporate the ether extract to a volume of about 10 cc., and finally complete the removal of ether in a stream of air. Add 25 cc. of neutral alcohol and titrate with tenth-normal sodium hydroxide, using phenolphthalein as the indicator. The amount of mandelic acid found corresponds to not less than 39 per cent (W/V) nor more than 41 per cent (W/V) of the undiluted syrup.

WYETH INCORPORATED, PHILADELPHIA

Syrup Ammonium Mandelate: 480 cc. bottles, accompanied by a supply of chlorphenol red test papers.

ALLERGENIC PREPARATIONS (See New and Nonofficial Remedies, 1944, p. 35).

The following additional pollen extracts have been accepted:

HOLLISTER-STIER LABORATORIES, SPOKANE, WASH.

Pollen Extracts: *Acacia, Alfalfa, Ash (White), Beech, Bermuda Grass, Careless Weed, Cedar (Mountain), Clover, Cocklebur, Corn, Cottonwood (Common), Dock (Yellow), Elm, Fescue (Meadow), Goldenrod, Johnson Grass, Kochia, Maple (Hard), Oak (White), Olive, Pine (Yellow), Short Ragweed, Sage (Common), Sage (Pasture), Sage (Prairie), Spear Scale, Sugar Beet, Sweet Vernal Grass, Sycamore, Walnut (English), Wheat (Cultivated), Western Water Hemp* and *Wormwood.*

CHORIONIC GONADOTROPIN (See New and Nonofficial Remedies, 1944, p. 445).

The following dosage form has been accepted:

GEORGE A. BREON & CO., INC., KANSAS CITY, MO.

Chorionic Gonadotropin, 1,000 and 5,000 International Units: 10 cc. vials. A powdered preparation of chorionic gonadotropin packaged in vials which, when treated with the accompanying 10 cc. of phosphate buffer solution, furnishes solutions having a potency of 100 and 500 international units per cubic centimeter, respectively.

DIPHTHERIA TOXOID (See New and Nonofficial Remedies, 1944, p. 560).

The following dosage form has been accepted:

NATIONAL DRUG CO., PHILADELPHIA

Diphtheria Toxoid (Fluid-Ramon): 30 cc. vials. Preserved with 1:10,000 merthiolate.

ANTI-ERYSIPELOID SERUM (See New and Nonofficial Remedies, 1944, p. 547).

The following dosage form has been accepted:

PITMAN-MOORE CO., INDIANAPOLIS

Anti-Erysipeloid Serum (Refined): 10 cc. vial. Preserved with merthiolate 1:10,000.

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SATURDAY, APRIL 7, 1945

A GROWTH PROMOTING SUBSTANCE FOR INDOLENT WOUNDS

In 1911 Carrel [1] employed embryonic tissue extract as the basic element in his tissue cultures. Saline extracts of proliferating tissues added to a culture medium, he found, increased the rate growth of cell colonies in vitro. Carrel believed that this growth promoting property was possessed by the embryonic tissue alone. Maximov, von Moelendorf and others demonstrated that extracts of adult tissue, which they used in their tissue culture experiments, likewise exhibited the growth stimulating property. However, the tissues with which they worked were of the growing type, either neoplastic or bone marrow. Carrel demonstrated in 1913 that extracts of adult tissues, such as the spleen, liver, connective tissue, kidney, heart, blood cells, thyroid and muscle, stimulated the growth of connective tissue cells in vitro.

Doljanski, Hoffman and Tenenbaum [2] demonstrated that extract of heart muscle of a hen exerted a pronounced growth stimulating effect on a culture of fibroblasts. This effect was much more pronounced than that of embryonal tissue derived from a 7 day old chick embryo. These authors further demonstrated that the growth promoting ability of adult tissue is not restricted to homologous cells but is present also in heterologous adult tissues. They further demonstrated that human epithelium in vitro is stimulated by extracts of heart muscle from adult fowl.

Waugh [3] described in 1940 the clinical application of "epicutan," an embryonic material prepared by an agency in Copenhagen. In 18 cases the time of healing, as determined by Du Nouy's formula, was reduced by 30 per cent. Goldberg [4] summarized two years' experience of Soviet clinicians with embryonic emulsions by stating that 15 or 25 per cent ointment appeared to stimulate the growth of epithelium and fibroblasts and that discharges from wounds diminished, granulation tissue appeared earlier and epithelization was prompt.

Mandl and Maybaum,[5] using a dry powder prepared from adult tissue extracts by the method of Werner and Doljanski, obtained healing in 65 out of 94 indolent wounds. They believed that the stimulating effect concerned the formation of granulation and probably even to a higher degree stimulation of epithelization. Kerr and Werner [6] have reported the use of a powdered preparation of sheep's heart prepared by Werner and Doljanski at the Department of Experimental Pathology of the Hebrew University, Jerusalem. The patients had infected, nonhealing ulcers; they were first subjected to accepted methods of treatment, such as occlusive, elastic dressings, sulfanilamide powder with tulle gras, petrolatum dressings, plaster of paris and skin grafting. Of 36 cases which fulfilled their criteria of intractability to orthodox methods, 33 fulfilled their criteria of success. These authors feel that no other method or combination of methods could have accomplished the same results within the periods quoted: recovery occurred in over 90 per cent of these 36 failures with the usual methods.

1. Carrel, Alexis, and Burrows, M. T.: Artificial Stimulation and Inhibition of the Growth of Normal and Sarcomatous Tissues, J. A. M. A. **56:** 32 (Jan. 7) 1911.
2. Doljanski, L.; Hoffman, R. S., and Tenenbaum E.: Effects of Extracts of Heterologous Adult Tissue on Cell Growth in Vitro and Their Use in Wound Healing, Nature, London **150:** 23 (July 4) 1942.
3. Waugh, W. G.: Experiments in the Acceleration of Wound Healing, Brit. M. J. **1:** 249 (Feb. 17) 1940.
4. Goldberg, D. I.: The Stimulation of Wound Healing by Embryonal Tissue, Am. Rev. Soviet Med. **2:** 225 (Feb.) 1945.
5. Mandl, F., and Maybaum, F.: Cell Growth Promoting Substances Derived from Adult Tissues in Wound Healing, Acta med. orient. **2:** 136 (Aug.-Sept.) 1943.
6. Kerr, A. B., and Werner, H.: The Clinical Value of a Growth Promoting Substance in the Treatment of Indolent Wounds, Brit. J. Surg. **32:** 281 (Oct.) 1944.

ASPERGILLUS ANTIBIOTICS (TUBERCULOCIDINS)

In 1942 Wilkins and Harris [1] of the Department of Botany, Oxford University, England, examined 100 species of fungi for the production of bacteriostatic or bactericidal substances, Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa being used as test organisms. About 25 per cent of the Penicillium strains and 40 per cent of the Aspergillus strains yielded antibiotics. Aspergillus fumigatus yielded particularly active filtrates, apparently superior to the bacteriostatic substances produced by Penicillium. From aspergillus filtrates Chain and his associates [2] of the Sir William Dunn School of Pathology, Oxford University, subsequently isolated a crystalline antibiotic, "helvolic acid," the name being derived from the variety of Aspergillus fumigatus yielding the best product.

This crystalline product is sufficiently stable to resist boiling for fifteen minutes. It inhibits the growth of gram positive organisms (including gas gangrene) in dilutions as high as 1:1,280,000. Its bacteriostatic power is not reduced by the presence of pus, serum

1. Wilkins, W. H., and Harris, G. C. M.: Brit. J. Exper. Path. **23:** 166, 1942.
2. Chain, E.; Florey, H. W.; Jennings, M. A., and Williams, T. I.: Brit. J. Exper. Path. **24:** 108, 1943.

or other normal or pathologic tissue products. The product is excreted in the urine much more slowly than penicillin. After a single intravenous injection an effective therapeutic level is maintained for over ten hours in the blood stream, penicillin disappearing within two hours. The substance is sufficiently low in toxicity to be of clinical promise. Injected into mice, "helvolic acid" has distinct therapeutic value in the treatment of experimental staphylocoecic or streptococcic infections.

A year later Waksman and his associates [3] of the New Jersey Agricultural Experiment Station demonstrated a somewhat similar substance in other varieties of Aspergillus fumigatus. This second product ("fumigacin") is both bacteriostatic and bactericidal for the routine test organisms and can be obtained in relatively pure form as needle shaped crystals from alcoholic solutions. Unfortunately it is so highly toxic as to be without practical clinical interest.

Research interest in aspergillus antibiotics was stimulated by the subsequent demonstration that other strains of Aspergillus yield products active against the tubercle bacillus. Soltys [4] of the Institute of Animal Pathology, Cambridge University, named his product "aspergillin." His product is inactive against staphylococci but inhibits the growth of Mycobacterium tuberculosis even when tested in high dilutions. Soltys's antibiotic is nontoxic for experimental animals and is sufficiently stable to withstand boiling for one hour.

More detailed studies of this (or a similar) tuberculocidal substance are now reported by Asheshov and Strelitz [5] of the University of Western Ontario, Canada. The Aspergillus fumigatus strain used by them was originally isolated as a laboratory contaminant. Grown at room temperature on Czapex-Dox medium containing 2 per cent corn syrup, the strain produces substances active against gram positive, gram negative and acid fast bacteria. After fifteen to eighteen days' growth the culture filtrate inhibits growth of staphylococci in a dilution as high as 1:40. Activity against Escherichia coli varied independently from this and was never higher than 1:20. The substance active against staphylococci is apparently identical with that active against acid fast bacteria. This tuberculocidal substance can be obtained in relatively pure form by extracting the culture medium with chloroform, or the substance may be adsorbed on animal charcoal and subsequently eluted with chloroform. As a third method, the substance may be precipitated with other products by saturating the culture medium with ammonium sulfate and then extracted from the mixed precipitate with chloroform.

Tuberculostatic action of this product was tested by serial dilutions of the resulting crude product in Kirchner's [6] medium and inoculating the tubes with a suspension of tubercle bacilli. Final examination for growth was made after six weeks. Thus tested, the partially purified substance inhibits the multiplication of human type tubercle bacilli in dilutions as high as 1:1,400,000. Tuberculocidal action was estimated by incubating a heavy suspension of tubercle bacilli with different dilutions of the substance for twenty-four hours and then testing quantitatively for viability. Thus tested, the crude product often kills human type tubercle bacilli in a dilution 1:500,000. Bacteriostatic or bactericidal action was not demonstrated with avian type tubercle bacilli.

Animal experiments on toxicity, topographic distribution and therapeutic activity have been postponed till this antibiotic can be obtained in greater purity. Several other as yet unidentified molds have been found to produce tuberculostatic and tuberculocidal substances of equal potency.

3. Waksman, S. A.; Horning, E. S., and Spencer, E. L.: J. Bact. **45**: 233, 1943.
4. Soltys, M. A.: Nature, London **154**: 550, 1944.
5. Asheshov, I. N., and Strelitz, F.: Science **101**: 119 (Feb. 2) 1945.

Current Comment

MORE LIFE FOR YOU

On page 930 of this issue of THE JOURNAL will be found an announcement of a new series of electrically transcribed radio programs made available on loan for use by local medical societies or by local public health agencies when approved by the local medical societies. "More Life for You in the Best Years of Your Life" is the theme and title of these programs, in which twenty-three prominent specialists are interviewed on health problems facing adults. These transcriptions added to other series, Dodging Contagious Diseases, Before the Doctor Comes, Medicine Serves America, Live and Like It, and a special series for elementary school use entitled Health Heroes, represent the development of an extensive coverage of the health field planned by the Bureau of Health Education under authorization of the Trustees of the American Medical Association. In addition to the series now available, which constitutes sixty-three weeks of continuous broadcasting exclusive of the Health Heroes series for schools, transcriptions planned and soon to be released include one on summer health hints under the title Keep Cool, ready about May 15, on public health problems, entitled Guardians of Your Health, ready approximately July 15, and a series in dramatized form dealing with mental adjustment problems under the tentative title In Step with Life. By the end of 1945 there will be available a sufficient supply of transcribed programs prepared by radio professionals from authentic medical sources to keep any local medical society or health department on the air continuously for more than two years with a minimum of local effort. If acceptance and use of these programs justifies, it is hoped to keep a continuous supply of new material available. Experience of more

6. Kirchner, O.: Zentralbl. f. Bakt., I. Orig. **124**: 403, 1932.

than one thousand local broadcasts from available platters in 1944 indicates that these transcriptions are meeting a need. With one third of available physicians in the armed forces, remaining doctors are too busy to write and broadcast health information. Yet there was never a time when medical advances, food shortages and other wartime factors rendered health education more essential than now. The American Medical Association is providing this growing library of electrically transcribed health broadcasts to keep our people informed through their local medical societies. They are made available without charge to any responsible local group approved by the county medical society; the only expense is the nominal cost of returning the used records.

GEORGE COLMER'S REPORT OF AN OUTBREAK OF EPIDEMIC POLIOMYELITIS IN 1841

In medical history epidemic poliomyelitis appears first in sporadic form. Characteristic deformities of the limbs have been found on Egyptian mummies, and they are clearly shown by the well known Egyptian stele of the eighteenth dynasty as well as on Spanish and other paintings several hundred years ago. Quite likely the brother of Catherine the Great was attacked and left a cripple when a year and a half old. He was born in 1734. And Walter Scott in 1773, when he was of the same age, suffered an attack which resulted in paralysis of the right leg. The descriptions by Underwood (1789) in England and Heine (1848) in Germany of the paralytic stages of poliomyelitis were based on observations of sporadic cases. These facts indicate the long existence of the virus of poliomyelitis over widely separated areas. Only since the latter part of the last century, beginning about 1881, has the epidemic form of the disease become known. Since then the number and the extent of the epidemics have steadily increased in the temperate zones. Of much interest is a definite outbreak of infantile paralysis recorded by George Colmer, 1807-1878, of Springfield, La., in 1841, whose report,[1] word for word, was as follows:

> Medical Notes. By George Colmer.—Paralysis in Teething Children.—Whilst on a visit to the parish of West Feliciana, La., in the fall of 1841, my attention was called to a child about a year old, then slowly recovering from an attack of hemiplegia. The people (who were people of intelligence and unquestionable veracity) told me that eight or ten other cases of either hemiplegia or paraplegia had occurred during the preceding three or four months within a few miles of their residence, all of which had either completely recovered or were decidedly improving. The little sufferers were invariably under two years of age, and the cause seemed to be the same in all—namely, *teething.*

Dr. Colmer was greatly beloved and respected as physician and citizen. Fortunately a good account of his life and work has now been published [2] and reveals need for further investigation. His note, frequently mentioned as the earliest report of epidemic poliomyelitis, illustrates again the wide spread of the virus of the disease.

1. Colmer, George: Paralysis in Teething Children, Am. J. M. Sc. **5**: 248, 1843.
2. Casey, A. E., and Hidden, E. H.: George Colmer and the Epidemiology of Poliomyelitis, South. M. J. **37**: 471 (Sept.) 1944.

RESEARCH COUNCIL TO INVESTIGATE PROSTHETIC DEVICES

At the request of the Surgeon General of the Army, as indicated elsewhere in this issue (Medicine and the War, page 925), the National Academy of Sciences and the National Research Council have organized a Committee on Prosthetic Devices. Here for the first time experts in the field of engineering will combine with surgeons and inventors to apply to the manufacture of artificial limbs the knowledge that has been gained in the fundamental sciences. The history of prosthetic devices indicates that there has been a failure to apply much of the knowledge that has become available. The tendency has been for manufacturers of devices to hold strictly to models which they have themselves developed and on which they might be able to establish patents. Brace makers and makers of artificial limbs frequently have held as trade secrets some of the improvements which they have developed and would teach them only to their own apprentices. Many new discoveries have been made in alloys of metals which would provide light weight, malleability, freedom from rust and other desirable factors. These have, however, been incorporated too infrequently in the making of prosthetic devices. The committee will aim to incorporate these new advances into the making of artificial limbs and to bring about as much standardization as possible in parts and mechanisms so as to assure simplification of maintenance and repair. The auspices under which this committee has been established and the inclusion of such names as those of Kettering, Magnuson, McClure and Wilson mean that progress will be made. The chairman is Dr. Paul E. Klopsteg, professor of applied science at Northwestern University, who gives assurance that the points of view of engineering, production, fitting and servicing, as well as the medical and surgical points of view, will prevail in the work of this committee.

HYPOTENSION IN CUNA INDIANS

Blood pressure readings were taken by Kean [1] according to the recommendations of the American Heart Association on 408 Cuna Indians ranging in age from 16 to 66 years. The average pressure in the entire group was 105.2 systolic and 69.3 diastolic. There was no tendency for the pressure to rise with age. The highest recorded were two systolic pressures of 144; all the others were below 140. Four Indians had diastolic readings between 90 and 99. A large proportion had a hypotension. Kean in previous studies showed that hypertension occurred seven times more frequently in West Indians (Negroes) than in Panamanians (mostly mestizos) living on the Isthmus of Panama. These figures, together with others previously obtained, suggest a fundamental difference between these peoples which leads to the development of hypertension in West Indians, a low incidence of hypertension in mestizos and the complete absence of what is considered high blood pressure in Cuna Indians.

1. Kean, B. H.: The Blood Pressure of the Cuna Indians, Am. J. Trop. Med. **24**: 341 (Nov.) 1944.

MEDICINE AND THE WAR

ARMY

A. A. F. CLINICAL REFRESHER TRAINING

The establishment of clinical refresher training for A. A. F. Medical officers returning from overseas and for others whose assignments have provided them a minimum of clinical experience has been announced by Major Gen. David N. W. Grant, the Air Surgeon of the Army Air Forces.

The training covers a twelve week period and consists of a two week didactic course at the A. A. F. School of Aviation Medicine, Randolph Field, Texas, and a ten week clinical course in one of the larger A. A. F. regional hospitals.

The purpose of the training, said General Grant, is to give medical officers who for a period of twelve months or more have had a minimum of active clinical work as the result of assignment to administrative, dispensary or tactical positions an opportunity (1) to study the newer methods of medical and surgical treatment and (2) to qualify for clinical positions in A. A. F. hospitals.

"It is the nature of war to prevent a great many of us from doing what we want to do," said General Grant. "Much of the flight surgeon's work is not medicine per se, yet the practice of aviation medicine is a vitally important mission requiring the scientific training and humanitarian interest of the medical officer and, with competent performance, constitutes preventive medicine of the highest order.

"The flight surgeon's success in the aero medical extension of the airman's sphere of action should be ample reward for any sacrifice of clinical interest. There have been complaints, however, that the flight surgeon does not find sufficient opportunity for enhancing his professional competence in clinical medicine and surgery. This is true. The wing, group or squadron surgeon who has been overseas for one, two or three years has had little or no opportunity for experience as a practitioner.

"A few tactical air forces which have hospital facilities as a part of their organization have been able to remedy this situation to a certain extent by rotating medical officers between field and hospital service."

For medical officers returning home, he said, clinical refresher training has been introduced in line with his long-held intent to do everything within his power to secure the futures of the men to whom he is personally as well as officially obligated for the outstanding success of the A. A. F. Medical Service.

The new postgraduate training in the A. A. F. is described as a logical sequence to the resident training provided for more than 600 young medical officers in A. A. F. hospitals accredited for this purpose by the Council on Medical Education and Hospitals of the American Medical Association.

The refresher training is given on a voluntary basis to officers for whom a hospital assignment is contemplated, preference being given to those with the longest terms of overseas service, regardless of rank.

If vacancies are not filled by returnees, medical officers assigned to administrative, dispensary or tactical positions in the zone of interior will be considered for this training.

The plan of training, as described in A. A. F. letter 50-97, dated Feb. 20, 1945, provides in the didactic phase for clinical conferences and lectures in medicine, surgery and the subspecialties, with parallel reading in textbooks and periodicals prescribed. In the second, or hospital, phase the student medical officers will perform the duties of ward officers, receive special instruction in x-ray interpretation and laboratory diagnosis and have opportunity to work in the operating room in such capacity as may be determined by the chief of surgery. All hospital training will be of an on the job character in which fullest utilization will be made of the officers' services for essential medical duties.

Facilities for training in the following specialties are available in A. A. F. hospitals: general medicine, cardiology, gastroenterology, dermatology, bacteriology, general surgery, anesthesiology, orthopedic surgery, otolaryngology, urology, ophthalmology, roentgenology and psychiatry.

"While the primary purpose of clinical refresher training is to prepare the medical officer for an A. A. F. hospital assignment, it is obvious that the offered course will be of postwar value to the individual," said General Grant.

ESTABLISH COMMITTEE ON PROSTHETIC DEVICES

A study of the problems associated with providing war veterans with artificial limbs has been initiated, on request of the Surgeon General of the Army, by the National Academy of Sciences and the National Research Council, through a newly established Committee on Prosthetic Devices. The committee will represent jointly the Division of Engineering and Industrial Research and the Division of Medical Sciences of the council, and its activities, including the necessary research entailed in the project, are supported by the Office of Scientific Research and Development, through the latter's Committee on Medical Research.

Chairman of the committee is Dr. Paul E. Klopsteg, professor of applied science at Northwestern University and director of research of the Northwestern Technological Institute. Dr. Klopsteg states that it is the intention of the committee to consider the problems from the points of view of engineering, production, fitting and servicing as well as from their medical and surgical aspects. Its purpose is to make certain that veterans will be provided with the best possible prosthetic appliances that can be devised.

In considering mechanisms and parts of limbs the committee has no intention of disregarding all the good work that has been done but, rather, it will analyze objectively every meritorious device. Any new development will begin on the foundation of experience already available, as manifested in the many ingenious mechanisms now in use and in the success that has been achieved in the fitting and use of limbs by both military and civilian personnel. Another aim of the committee is to bring about as much standardization as possible in parts and mechanisms, to assure simplification of maintenance and repair.

In view of the magnitude of the task, the work being undertaken by the committee is expected to continue for many months; but it is likely that results and findings that may be immediately applicable will be released as soon as they are available. To assure the utmost utility and practicality of any developments done under the auspices of the committee, close working relationships are being established with government amputation centers in the hospitals of the armed forces.

Serving with the chairman are the following committee members: Dr. Harold Conn, surgeon in chief, Goodyear Tire & Rubber Company, Akron, Ohio; Mr. Mieth Maeser, research engineer of the United Shoe Machinery Corporation, Beverly, Mass.; Dr. Paul B. Magnuson, chairman of the Department of Bone and Joint Surgery, Northwestern University Medical School, Chicago; Dr. Robert R. McMath, director of the McMath-Hulbert Observatory of the University of Michigan; Mr. Edmond M. Wagner, chief of the engineering section of the National Defense Research Committee, Washington, D. C., and Dr. Philip Wilson, clinical professor of Orthopedic Surgery, Columbia University College of Physicians and Surgeons, New York.

Dr. Charles F. Kettering, head of General Motors Research Division, Detroit, and Dr. Roy D. McClure, chief surgeon of Henry Ford Hospital, Detroit, are consultants to the committee.

The operating headquarters of the committee are at Northwestern University, Evanston, Ill.

FIVE ARMY NURSES DECORATED, ONE COMMENDED

The War Department recently announced that five members of the Army Nurse Corps have been decorated and one has been awarded a commendation for professional skill, determination and high sense of service exhibited.

Major Louise M. Fitzgerald, Jacksonville, Fla., was awarded the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding service as chief of the Nurse Section, Headquarters, Persian Gulf Command, from July 15, 1943 to May 26, 1944. She contributed in a high degree to the success of the mission of the command by establishing the administration, training and control of the members of the Army Nurse Corps of that command and by keeping the morale of the command at a high level in spite of great handicaps.

First Lieut. Retha O. Rodgers of Hubbard, Iowa, and 1st Lieut. Joseph F. Sansone of Milwaukee were awarded the Air Medal for services rendered while acting as flight nurses from Feb. 21, 1943 to July 23, 1944 on unarmed and unarmored troop carrier aircraft on air evacuation missions in the Mediterranean and European theaters of operation. They administered to the needs of wounded personnel being evacuated from combat zones in near areas in the Mediterranean and European theaters of operation. They administered to the needs of wounded personnel being evacuated from combat zones in rear areas in the Mediterranean theater and in northern France. Their aircraft was subjected to the risk of attack from enemy ground installations and hostile aircraft. They are also credited with the training of a large number of air evacuation nurses.

Second Lieut. Bernice V. McDonald of Burkburnett, Texas, as flight nurse from Feb. 19, 1944 to July 31, 1944 with the Army Air Forces was awarded the Air Medal Sept. 25, 1944 for distinguishing herself by meritorious achievement while participating in more than one hundred and fifty hours of operational flight in transport aircraft through the combat zones of Upper Assam, Burma and Southwest China. She helped evacuate sick and wounded from forward air strips in Burma to hospitals in India and China.

Second Lieut. Ruth C. Bimber of Beaver Falls, Pa., was awarded the Soldier's Medal on Sept. 6, 1944 for heroism July 11, 1944. While swimming with a party of officers from her unit, two officers were caught in a treacherous undertow. Lieutenant Bimber quickly went to the help of one of the officers but because of the strong current and rough surf she was unable to tow him to shore. She held his head out of the water until another officer came to her assistance.

First Lieut. Ledore G. Alsup of Fort Worth, Texas, was awarded a commendation on July 9, 1944 for her courageous actions on March 29, 1944 near Anzio, Italy, when she was responsible for the safety of her patients while removing them to safer positions.

CONSTRUCTION OF GENERAL HOSPITAL FACILITIES AT BROOKE GENERAL HOSPITAL

The War Department recently announced the authorization for the construction of general hospital and convalescent hospital facilities at Brooke General Hospital, Fort Sam Houston, Texas. The construction authorized includes conversion of the redistribution center area, including utilization of fifteen 63 man barracks and consolidation of several other buildings into mess halls and service buildings, installation of operating rooms and clinical facilities and other facilities to provide 1,700 additional beds. Convalescent facilities for 5,000 men will be provided. The work will be supervised by the San Antonio District Office of the Corps of Engineers.

MAJOR EMIL P. REED RESCUED

Among those rescued recently in the Philippines was Major Emil P. Reed, formerly of Brownsville, Texas. Dr. Reed graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1931 and entered the service Nov. 8, 1940.

EXPERIMENTAL ORTHOPEDIC FOOTWEAR CLINIC

Anticipating the need for special footwear for soldiers returning from overseas with foot injuries, the Office of the Quartermaster General, in cooperation with the Office of the Surgeon General, has authorized an experimental cast making unit and orthopedic footwear clinic at the Boston Quartermaster Depot. Accurate casts will be made of deformed feet, and permanent metal molds will be fashioned from these casts. The wooden lasts on which the shoes are built are made from these molds. Casts, molds, lasts and patterns will be marked with the name and serial number of the soldier and held at the depot. Thus, through his Veterans Bureau, the injured man will be able to obtain the special shoes as long as he needs them. The plan calls for the establishment of similar clinics in each service command in the United States.

ARMY AWARDS AND COMMENDATIONS

Major James E. Crane

Major James E. Crane of Stamford, Conn., flight surgeon at the Fort Logan Convalescent Hospital, was recently awarded the Bronze Star for his work in the field of aviation medicine. He was cited for "meritorious service in the South Pacific from Jan. 2, 1943 to May 1, 1944. He commanded the first medical air evacuation transport squadron to function in any theater of war and with limited personnel and equipment quickly developed a smooth running unit which met every demand incident to the evacuation of casualties by air from the combat area. Later, as flight surgeon of the Army Air Corps Rehabilitation Center in New Zealand, his professional skill and wide experience in the field of aviation contributed much to the personal welfare and fighting spirit of flying personnel suffering from the strain of sustained combat who passed through the center." Dr. Crane graduated from the University of Vermont College of Medicine, Burlington, in 1939 and entered the service in February 1941.

Colonel Rexford L. Diveley

The Bronze Star with a special citation was recently awarded to Col. Rexford L. Diveley, formerly of Kansas City, Mo., "for meritorious service in connection with military operations as a senior consultant, Orthopedic Surgery Office of the Chief Surgeon, EPO, on the 25th of August to the 15th of May 1944. Col. Diveley is responsible for development of convalescent and rehabilitative facilities for orthopedic patients." Dr. Diveley graduated from the University of Kansas School of Medicine, Kansas City, in 1917 and entered the service July 22, 1942.

Major Sol I. Frankel

Major Sol I. Frankel, St. Louis, former regimental surgeon with an infantry division in Italy, now stationed at an army camp in Washington, was awarded the Bronze Star for meritorious service in action near Santa Maria Infante last May. Dr. Frankel graduated from St. Louis University School of Medicine in 1924 and entered the service June 19, 1943.

Major Irving Favus

The Bronze Star was recently awarded to Major Irving Favus, formerly of Chicago, for "meritorious service." He is serving in General Patton's Third Army and was decorated January 15. Dr. Favus graduated from the University of Illinois College of Medicine, Chicago, in 1937 and entered the service Jan. 25, 1941.

Lieutenant Colonel George C. Bess

Lieut. Col. George C. Bess, formerly of St. Louis, has been given the second Distinguished Service Badge. He was former chief surgeon of a heavy bomber group but is now serving as chief medical inspector of the Fifteenth Army Air Force in Italy. Dr. Bess graduated from St. Louis University School of Medicine in 1935 and entered the service April 15, 1941.

NAVY

NAVY PUBLIC HEALTH UNIT TO AID GREEK GOVERNMENT

At the request of the Greek government, a navy public health unit left recently for Athens to curb disease, restore and improve sanitary facilities, disseminate public health education and do everything else in its power to ameliorate living conditions among the people crushed by years of enemy occupation. The unit of fourteen men is under the command of Comdr. Theodore R. Meyer of Sag Harbor, Long Island, N. Y. Functioning directly under the naval attaché to the American embassy in Athens, the public health group will direct its attack particularly against tuberculosis, typhoid, malaria, syphilis, typhus and trachoma. The lack of adequate food, clothing, housing, hospitals and sanitary facilities has precipitated conditions whose correction and relief are expected to tax the naval "trouble shooters" to the utmost. With them they took more than a ton of chemicals, drugs, biologic products and other supplies, to be replenished as warranted. Lieut. Comdr. W. J. Dougherty of Beverly Farms, Mass., is second in charge of the unit.

NAVY AWARDS AND COMMENDATIONS

Lieutenant Commander Warren Elmer Page

The Silver Star Medal was recently awarded to Lieut. Comdr. Warren Elmer Page, formerly of Oakland, Calif. The citation accompanying the award read "for conspicuous gallantry and intrepidity while serving with a marine force during an aerial attack by enemy Japanese forces at Bougainville, Solomon Islands, on the night of Nov. 7, 1943. Injured and dazed by an exploding bomb, Lieutenant Commander Page heroically left his protected position and rushed to the assistance of the wounded. Working tirelessly in complete darkness and in the face of high explosives and bomb fragments, he fearlessly went from place to place, skilfully administering medical aid to his injured comrades and, with the assistance of a hospital corpsman, moved them to a protected location. His expert professional ability, brilliant initiative and great personal valor in voluntarily risking his life for others directly contributed to the saving of many men and were in keeping with the highest traditions of the United States Naval Service." Dr. Page graduated from the University of Oregon Medical School, Portland, in 1927 and entered the service Oct. 19, 1942.

Lieutenant Commander Justin Mooney

The Bronze Star was recently presented to Lieut. Comdr. Justin Mooney, formerly of Kansas City, Mo. According to the citation accompanying the award, "he distinguished himself by heroic and meritorious conduct in action with the enemy during a series of air raids on Oct. 27, 1944 on ships at anchor near his ship. He boarded a burning gasoline ship as a member of a fire and rescue party. After ascertaining that casualties were taken care of, he remained on deck and assisted in fighting the blazing gasoline fire. During this period, which was at night, the ship was a natural target for the expected air raids. His actions throughout distinguished him among those performing duties of the same character." Dr. Mooney graduated from the University of Michigan Medical School, Ann Arbor, in 1924 and entered the service Feb. 21, 1944.

Lieutenant Commander Marcel L. Mooney

Lieut. Comdr. Marcel L. Mooney, formerly of Kansas City, Mo., was recently awarded the Bronze Star with the citation that "he distinguished himself by heroic and meritorious conduct in action with the enemy during a series of air raids on Oct. 27, 1944 on ships at anchor near his ship. He boarded a burning gasoline ship as a member of a fire and rescue party. After ascertaining that casualties were taken care of, he remained on deck and assisted in fighting the blazing gasoline fire. During this period, which was at night, the ship was a natural target for the expected air raids. His actions throughout distinguished him among those performing duties of the same character." Dr. Mooney graduated from the University of Michigan Medical School, Ann Arbor, in 1931 and entered the service Oct. 7, 1942.

Lieutenant (jg) Robert Thomas Browne

The Navy Cross was recently presented to Lieut. (jg) Robert Thomas Browne, formerly of Peoria, Ill., "for extraordinary heroism while attached to the U. S. S. *Johnston* in action against enemy Japanese forces off the Island of Samar during the second battle of the Philippines on Oct. 25, 1944. Acting with cool initiative when the abandon ship order was given, Lieutenant, Junior Grade, Browne remained on board the *Johnston* supplying injured men with life jackets, assisting to evacuate them from the stricken vessel and ministering to the wounded in the face of terrific salvos from hostile gun batteries. A calm and courageous leader, Lieutenant, Junior Grade, Browne served as an inspiring example of fortitude and loyalty throughout the bitter engagement with powerful units of the Japanese fleet. By his gallant spirit of self sacrifice he rendered valiant service to his shipmates at extreme risk to his own life and upheld the highest traditions of the United States Naval Service." Dr. Browne graduated from the University of Illinois College of Medicine in 1942 and entered the service July 10, 1943.

Lieutenant Commander Horace Martin Gezon

The Legion of Merit was recently awarded to Lieut. Comdr. Horace Martin Gezon, formerly of Grand Rapids, Mich., "for exceptionally meritorious conduct in the performance of outstanding services to the government of the United States as officer in charge of the Epidemiology Unit of United States Naval Forces, Northwest African Waters, during a typhus epidemic in Naples, Italy, in January 1944. Charged with the vital task of checking a potential typhus epidemic, Lieutenant Commander (then Lieutenant) Gezon performed the exacting duties of his responsible office conscientiously and with untiring effort, skilfully determining and checking the cause of the malady. On one occasion, when a case of typhus on board a merchant ship was suspected, he personally effected preventive measures and inoculated the entire ship's company. Lieutenant Commander Gezon's expert professional ability and loyal devotion to duty throughout this crucial period contributed materially to the successful arresting of the typhus epidemic and the probable saving of many lives." Dr. Gezon graduated from the University of Chicago School of Medicine in 1940 and entered the service in April 1942.

Lieutenant William C. McClure

Lieut. William C. McClure, formerly of Oklahoma City, was recently awarded the Bronze Star "for meritorious achievement in action against the enemy as regimental surgeon of a Marine infantry regiment on Saipan, and Tinian, Marianas Islands, from June 15 to Aug. 10, 1944. By his cool and capable handling of evacuation facilities and by his experience in the care of the wounded, he was largely instrumental in saving the lives of many badly wounded Marines who might otherwise have died. He displayed great coolness under fire and his conduct throughout was in keeping with the highest traditions of the United States Naval Service." Dr. McClure graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1936 and entered the service March 9, 1942.

Captain Cornelius A. Mahoney

The Silver Star was recently awarded, at the recommendation of the Navy, to Capt. Cornelius A. Mahoney of the Army Medical Corps. The award was made "for conspicuous gallantry and intrepidity in action while serving as ship's surgeon aboard the U. S. S. LST 315 during the amphibious invasion of Sicily in July 1943." The citation states that "when a fierce enemy attack left his vessel raging with fires and explosions, making abandonment necessary, Captain Mahoney steadfastly remained on board with utter disregard for his own personal safety to assist in transferring all wounded to another ship, leaving the stricken vessel only when his task had been accomplished. Captain Mahoney's tenacious devotion to duty and cool courage in the face of grave peril undoubtedly saved the lives of many men who otherwise might have perished and were in keeping with the highest traditions of the United States Naval Service." Dr. Mahoney graduated from St. Louis University School of Medicine in 1937 and entered the service in April 1941.

MISCELLANEOUS

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

Nebraska

A. A. F. Regional Hospital, Lincoln: Sarcoidosis, Dr. Olin J. Cameron, April 10; Electrostethography: The Possible Clinical Value of Visualizing Chest and Heart Sounds, Dr. F. Lowell Dunn, April 10; Clinical Pathologic Conference, Dr. James Tollman, April 10.

California

Birmingham General Hospital, Van Nuys: Infections of the Mandible, Lieut. E. J. Durling, April 11.

U. S. Naval Hospital, Oceanside: Atypical Pneumonias, Dr. W. E. Macpherson; X-Ray Observations, Dr. Walter Stilson, April 12.

U. S. Naval Hospital, Corona: Intestinal Obstruction Due to Regional Enteritis, Lieut. Col. William G. Sheehan; X-Ray Observations, Major Ralph Pomeranz, April 12.

Illinois

Gardiner General Hospital, Chicago: Malignancies in the Army Age Group: Medical X-Ray and Surgical Diagnosis and Treatment, Drs. Alexander Brunschwig and James P. Simonds, April 11; Management of Malignant Tumors in the Army Age Group, Dr. Danely Slaughter, April 18; Endocrinology, Dr. Willard O. Thompson, April 25.

Station Hospital, Fort Sheridan: Virus and Rickettsial Diseases: Medical and Neurologic Diseases and Treatment, Dr. Francis Gordon and Comdr. W. G. Reddick, April 12; Psychosomatic Medicine, Drs. David Slight and Francis J. Gerty, April 26.

Vaughan General Hospital, Hines: Thrombosis, Thrombophlebitis and Anticoagulants in the Less Common Peripheral Vascular Diseases, Drs. Theodore R. Van Dellen and George W. Scupham, April 11; Tropical Ulcer, Capt. Walter W. Tobin, April 13; Psychosomatic Medicine, Dr. Francis J. Gerty, April 18; Clinicopathologic Conference or X-Ray Conference, Major V. P. Graham, April 18; Ménière's Syndrome, with Case Presentation, Major S. R. Grimes, April 20; Peptic Ulcer, Gallbladder and Liver Diseases, Drs. Lowell D. Snerf and Lester R. Dragstedt, April 25; Newer Concepts of the Treatment of Congestive Heart Failure, Capt. L. M. Schweiger, April 27.

U. S. Naval Hospital, Great Lakes: Nerve and Tendon Injuries, Dr. Sumner L. Koch, April 17.

Mayo General Hospital, Galesburg: Wound Healing and Tendon Surgery, Drs. Hilger P. Jenkins and Sumner Koch, April 11; Mental Hygiene and the Prevention of Neuroses in War, Capt. Charles O. Sturdevant, April 25.

Station Hospital, Camp Ellis, Lewistown: Low Back Pain, Drs. Fremont A. Chandler and Adrien Verbrugghen, April 11; Chest Diseases and Diseases of the Larynx, Drs. Robert G. Bloch and Paul H. Holinger, April 25.

Wisconsin

Station Hospital, Truax Field: Blood Dyscrasias, Dr. Frederick W. Madison, April 11; Diseases of the Kidneys and Urogenital Tract, Dr. Francis D. Murphy, April 25.

BOOKS FOR THE COLLEGES OF DENMARK

In October 1943 a nonprofit, temporary organization, "Books for the Colleges of Denmark," % General Medical Library, 333 Cedar Street, New Haven, Conn., was started in New York with the purpose of collecting funds for the purchase of the scientific periodicals and books which have been published in this country since 1940. When the war is over the accumulated material is to be presented to Denmark as a gift to the public and scientific libraries of that country. The organization is sponsored by His Excellency Henrik Kauffmann, the Danish minister to the United States, and by the American Scandinavian Foundation.

CONFERENCE AT TORNEY GENERAL HOSPITAL

A two day medical-surgical conference for medical officers was recently held at Torney General Hospital, Palm Springs, Calif., at which specialists in every branch of medicine and surgery representing army and naval hospitals throughout the Ninth Service Command area attended and participated. Col. A. B. Jones, commanding officer of the Torney General Hospital, opened the conference with an address of welcome. Many papers were read and discussed on various subjects, and clinical exhibits were arranged by 2d Lieut. Carroll N. Jones Jr., M. A. C.

MEDICAL AND SURGICAL RELIEF COMMITTEE

In a recent report published by the Medical and Surgical Relief Committee of America (420 Lexington Avenue, New York 17), an eleemosynary organization, it was stated that over $12,000 worth of medical supplies were donated to people here and abroad. Topping the list of foreign shipments was France, with supplies amounting to more than $8,300, sent to three different centers, and a fourth shipment on its way to Algeria and southern France for the use of soldiers and families of prisoners of war. In addition to medical supplies and equipment, this last consignment contains baby foods, apples and apricots, handkerchiefs and 10,000 vitamin capsules.

HOSPITALS NEEDING INTERNS AND RESIDENTS

The following hospitals have indicated to the Council on Medical Education and Hospitals that they have not completed their house staff quota allotted by the Procurement and Assignment Service:

(Continuation of list in THE JOURNAL, March 31, page 859)

DELAWARE

Wilmington Delaware Hospital, Wilmington. Capacity, 224; admissions, 4,267. Mr. T. A. Weth, Superintendent (1 intern).

ILLINOIS

Jackson Park Hospital, Chicago. Capacity, 226; admissions, 4,958. Mr. L. W. Hilton, Superintendent (interns).

INDIANA

St. Joseph's Hospital, South Bend. Capacity, 218; admissions, 5,393. Sister Mary Ellen, Superintendent (2 interns, July 1).

MARYLAND

Johns Hopkins Hospital, Baltimore. Capacity, 1,034; admissions, 18,214. Dr. Winford H. Smith, Director (residents—otolaryngology and radiology, July 1).

MICHIGAN

City of Detroit Receiving Hospital, Detroit. Capacity, 640; admissions, 17,540. Dr. R. R. Piper, Medical Superintendent (2 interns).

MISSOURI

St. Louis City Hospital, St. Louis. Capacity, 1,104; admissions, 14,098. Dr. Leo J. Wade, Medical Director (resident—psychiatry, July 1, disqualified for military service).

NEW YORK

Kingston Hospital, Kingston. Capacity, 123; admissions, 2,510. Miss Jessie P. Allan, Superintendent (resident—mixed service, October 1).

Bronx Hospital, New York City. Capacity, 389; admissions, 7,766. Mr. William B. Seltzer, Superintendent (resident—surgery, July 1, disqualified for military service).

St. Francis Hospital, New York City. Capacity, 441; admissions, 6,788. Sister Camilla, R.N., Superintendent (interns, July 1).

OHIO

St. Thomas Hospital, Akron. Capacity, 235; admissions, 6,147. Sister M. Eleanor, R.N., Superintendent (2 interns; 2 residents, disqualified for military service).

PENNSYLVANIA

Chester Hospital, Chester. Capacity, 270; admissions, 6,858. Mr. L. P. Wray, Superintendent (interns).

Chestnut Hill Hospital, Philadelphia. Capacity, 140; admissions, 2,795. Mr. H. P. Glendinning, Administrator (3 interns, July 1).

WISCONSIN

Madison General Hospital, Madison. Capacity, 203; admissions, 6,569. Miss Grace Croft, Administrator (resident—mixed service).

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

April 2, 1945.

World Health Department to Be Discussed at San Francisco

Second in importance to world peace will be plans for an international health organization to be discussed at the United Nations conference in San Francisco, Washington authorities believe. Foreign Policy Association experts express the view that such a health agency would rank next to military precautions as a means of maintaining peace. Health authorities recall the influenza epidemics that followed the first world war and point out that such developments as DDT and penicillin have helped to keep down disease in this war. Recent world health surveys point to the need of coordination of health control measures. Tuberculosis has become prevalent in devastated areas. Malnutrition is widespread. Breakdown of sanitation in bombed areas is a great potential peril to world health. Even before this war malaria, tuberculosis, nutritional diseases, syphilis and other diseases took heavy tolls in such countries as China and India.

Price of Penicillin Reduced as Production Increases

Since the release on March 15 of penicillin for civilian use the price of the drug has dropped as a result of sales competition and increased production, a check with official sources here reveals. Where $2.40 was charged for 100,000 Oxford units, the price for this quantity is now as low as $1.54, wholesale. Price to a physician ranges from $1.80 to $2 for 100,000 units. The OPA ceiling price of $10 per hundred thousand units has not been changed. It is estimated that the OPA in two months will have sufficient price data on hand to analyze costs in order to set a new ceiling. Should production continue to rise, another reduction in price is expected. The ultimate price of penicillin will be determined by success in finding improved methods of production and will depend on trade conditions generally. The prices of the sulfonamides are lower than those of penicillin. The District of Columbia Medical Society and the Army Medical Corps have issued a warning that penicillin is not a cure-all and have explained that it is issued in capsules for purchase on a doctor's prescription. People were advised to consult their physicians about its use.

Bill Proposing Aid for Neuropsychiatric Outclinics

Federal provision for outclinic treatment of neuropsychiatric patients, as advocated by the National Committee for Mental Hygiene, is proposed in bill H. R. 2550, known as the National Neuropsychiatric Bill, introduced in Congress by Representative J. Percy Priest, Democrat of Tennessee. The bill is to provide for, foster and aid in coordinating research relating to neuropsychiatric disorders, to provide for more effective prevention, diagnosis and treatment and to establish the National Neuropsychiatric Institute as a function of the U. S. Public Health Service. A central research hospital near Washington is proposed, as well as support to universities and hospitals in psychiatric research. States would be enabled to initiate service to patients, now emphasized by needs of medically discharged veterans.

Warning on Dangers of Nurse Draft is Given

Drafting nurses only for the armed forces will merely place an additional hardship on all civilian hospitals, Dr. Arthur J. Will, director of hospitals for Los Angeles County, said in a statement given to the Senate Military Affairs Committee during hearings on the House approved nurse draft bill. He said that voluntary recruiting of nurses not only had failed to meet the Army's urgent combat needs but has had the effect of curtailing the number of nurses available to civilian hospitals. Most of the nurses, he said, who had gone into the armed forces have come from the comparatively small number in hospitals. The alternative might be the registration of all graduate nurses, regardless of age, to the end that many who are now engaged in the practice of nursing could be drawn into civilian hospital work. The American Nurses Association announced that nurses now are applying for army service at the rate of seven hundred a week.

Veterans Administrator Hines Comments on Statement in The Journal

Commenting on an editorial in THE JOURNAL which reviewed reports made by the Senate Subcommittee on Health and Education and by newspapers and magazines on conditions in veterans' hospitals, Brig. Gen. Frank T. Hines, Veterans Administrator, said that he found the A. M. A. attitude "difficult to understand." He said "When THE JOURNAL criticizes the medicine being practiced in Veterans Administration hospitals, it is reflecting on its own membership, which directly contributed . . . to the clinical practices followed in caring for veterans." He stated that Veterans Administration medical officers and its entire special medical advisory group are members of the American Medical Association. The House, meantime, has passed a resolution authorizing its Committee on Veterans Affairs to investigate charges of "intolerable conditions" in Veterans Administration hospitals. It was passed on a roll call vote of 256 to 4 after Representative Philip J. Philbin, Democrat of Massachusetts, had urged the chamber to vote it down. Representative Philbin asked that the inquiry be extended to army and navy hospitals, which he said had also been accused of mistreating disabled and wounded veterans.

Rockefeller Grant Aids War Research Workers

A Rockefeller Foundation grant of $335,000 to the National Research Council will enable civilian and service war research workers to continue graduate school studies. A national but temporary program of postwar predoctoral fellowships is proposed to encourage resumption of graduate study in natural sciences for those who have had their education interrupted by war work. Cash value of the fellowships will permit those receiving them to devote substantially full time to working for Ph.D. degrees. The Washington announcement stated that "the almost complete cessation of consecutive professional training which has occurred in scientific fields will make impossible for some time the normal accession of additional highly trained personnel. These losses, in the face of sharply increasing demands for personnel, will inevitably retard to the danger point the resumption of scientific progress after the war. The resulting handicap to postwar industrial recovery, public health and military security is of national concern."

Twenty-One States Represented at Public Health Series

Women health chairmen from twenty-one states attended a Public Health Service course arranged by the General Federation of Women's Clubs and the U. S. Public Health Service at the Public Health Center, Bethesda, Md. Among speakers were Surg. Gen. Thomas Parran, Dr. Mayhew Derryberry, chief, Field Activities in Health Education; Dr. C. L. Williams Sr., associate chief, Bureau of State Services, with G. S. J. Perrott and Mrs. Marjorie B. Illig of Massachusetts, national chairman of the health committee, General Federation of Women's Clubs, presiding. Also heard were Dr. R. R. Spencer, chief, National Cancer Institute, and Dr. L. L. Williams Jr., medical director, Tropical Disease Section, U. S. Public Health Service.

Capital Notes

The Montgomery County Welfare Board has decided to collect fees from operators of nursing homes according to the number of patients.

District of Columbia commissions will ask funds from Congress to continue the psychiatric clinic at Juvenile Court, naming Dr. John F. Owen, superintendent of the State Hospital at Raleigh, N. C., as mental hygiene chief.

The Senate has passed a House bill permitting Georgetown University to erect its new hospital to a maximum height of 110 feet, which is over the usual zoning limitations.

In the cause of community health, the District has ordered Clean-Up Week from March 30 through April 7 at the request of civic groups led by Georgetown associations.

Leo G. Schmelzer, administrator of the Wisconsin General Hospital, Madison, Wis., will report here soon as superintendent of the New George Washington University Hospital.

Adequate supplies of poultry for convalescent patients in District hospitals has been pledged by poultry wholesalers here at a conference to discuss the current shortage.

An epidemic of dog bites prompts District Health Commissioner George Ruhland to brand the outbreak as "damnable." In the past two years rabid dogs have bitten more than 300 Washingtonians, 4 of whom died.

The first health education institute for ministers of all denominations has been held in Washington with panel discussions on tuberculosis, cancer, heart disease and community health.

Health requirements of the underprivileged of Washington have been surveyed by Community Chest directors in an effort to collect all possible data for postwar community needs.

Twenty-two veterans from various parts of the country have been hospitalized at the new Fort Washington, Md., facility of the Veterans Administration, which will have some 1,300 domiciliary beds and 65 hospital beds.

Four psychiatric and medical leaders who have given important assistance to the armed forces were elected to membership in the National Committee for Mental Hygiene, reports Dr. George S. Stevenson, medical director. They are Lieut. Col. Paul L. Schroeder, psychiatric consultant to Army Service Forces, Atlanta, Ga.; Capt. Francis J. Braceland of the Navy Bureau of Medicine and Surgery, Washington, D. C.; Dr. Raymond W. Waggoner, chairman, Department of Psychiatry, University of Michigan, Ann Arbor, who formulated the medical survey program used in Selective Service, and Lieut. Col. Louis H. Renfrow, executive officer, Medical Division, National Headquarters of Selective Service, Washington, D. C.

Representative O'Toole, Democrat of New York, has asked for a Congressional investigation into Sister Kenny's decision to leave the country, following her dispute with members of the pediatric staff of Minneapolis City Hospital and the University of Minnesota over her right to treat spastic cases.

District Commissioner Mason has charged that the old Municipal Tuberculosis Hospital on Upshur Street Northwest is being conducted as "a flophouse for people who go out for a day's work and then come back at night for a free meal and bed." He asked that it be closed.

Official Notes

A NEW SERIES OF ELECTRICAL TRANSCRIPTIONS

The Bureau of Health Education announces a new series of electrical transcriptions available April 1. The title of this series is "More Life for You," and its theme is health problems in adult life.

This series of transcriptions consists of thirteen programs of fifteen minutes each designed for broadcasting at weekly intervals. Each program is complete in itself. Introductory and closing announcements are furnished on script for the use of the announcer in the local radio station. The remainder of the program is on transcription. The form of these broadcasts is interview or round table followed by a summary. The broadcasters are twenty-three leading medical authorities interviewed by Harriet Hester. The programs are summarized by Dr. W. W. Bauer.

Following is the list of titles and participating experts:

1. Why We Grow Old. Dr. A. C. Ivy, Northwestern University; Dr. Arno B. Luckhardt, University of Chicago.
2. Diet and Food. C. A. Elvehjem, Ph.D., University of Wisconsin; Dr. J. S. McLester, Chairman, and Dr. George K. Anderson, Secretary of the Council on Foods and Nutrition of the American Medical Association.
3. Glands. Dr. E. L. Sevringhaus, University of Wisconsin; Dr. Austin E. Smith, Secretary of the Council on Pharmacy and Chemistry of the American Medical Association.
4. The Skin and Its Care. Dr. Clark W. Finnerud, University of Illinois.
5. Mental Health. Dr. Jules Masserman, University of Chicago.
6. Heart Disease. Dr. Edwin P. Jordan, Assistant Editor of THE JOURNAL; Dr. W. W. Bauer, Director of the Bureau of Health Education of the American Medical Association.
7. Cancer. Maude Slye, Ph.D., University of Chicago; Dr. Max Cutler, Chicago Tumor Institute; Dr. Frank L. Rector, Michigan Department of Health.
8. Kidney Disease. Dr. Herman L. Kretschmer, University of Illinois; Dr. George E. Coleman, Northwestern University.
9. Blood Pressure. Dr. Nathan S. Davis III, Northwestern University.
10. Jobs and Health. Dr. Stanley J. Seeger, Chairman, and Dr. Carl M. Peterson, Secretary of the Council on Industrial Health of the American Medical Association; Dr J. G. Townsend, U. S. Public Health Service.
11. Arthritis. Dr. Ernest E. Irons, University of Illinois.
12. Safety and Accident Prevention. Ned H. Dearborn, National Safety Council; Dr. Carl M. Peterson; Dr. W. W. Bauer.
13. Living Successfully. Dr. Morris Fishbein, Editor of THE JOURNAL.

This series is available on loan to local medical societies or to other local public health agencies subject to the approval of the local medical society. Make requests to the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago 10.

SCRIPTS FOR DOCTORS LOOK AHEAD

The basis of radio programs, whether they are talks, interviews or dramatizations, is the script. Scripts for Doctors Look Ahead are written by an experienced script writer, William J. Murphy, continuity editor of the National Broadcasting Company, Central Division, since 1940. Mr. Murphy is a cum laude graduate of Notre Dame University and is experienced as an advertising copy writer and radio continuity editor, having served as a continuity editor for the Columbia Broadcasting System prior to his National Broadcasting Company affiliation.

Mr. Murphy has written such well known features as Young Hickory, The Kilmer Family, Cameos of New Orleans, This Amazing America and all but two of the American Medical Association network broadcasts with NBC including such successful series as Medical Emergencies, Medicine in the News, Doctors at War, Doctors at Work and the electrically transcribed series Live and Like It.

The preparation of a script for Doctors Look Ahead begins with the selection and assembling of material by the Bureau of Health Education. A conference is then held in which the writer is given scientific material, an outline of the purposes of the broadcast and the special points to stress. Approximately a week later he returns with his dramatic script, for the plotting of which he is solely responsible. This script is then checked for script accuracy, ethics and similar considerations by the Bureau of Health Education and submitted to another medical consultant in the headquarters building for an unbiased opinion from one not concerned with preparing the script. When finally approved the designated physician either of the headquarters staff or an invited guest writes the closing summary and then the script is sent to the National Broadcasting Company for production.

In the next three weeks Doctors Look Ahead will include the following programs:

April 7. The Tuberculosis Situation in Wartime and Postwar, with particular reference to drug therapy.

April 14. Cancer, with special reference to education for youth. Summary will be by Dr. Frank L. Rector, cancer consultant, Michigan Department of Health.

April 21. Battle Fatigue, a program devoted to the effects of battle dangers and stress other than physical wounds. A special speaker to be announced.

Doctors Look Ahead will be heard on one hundred and twenty-three stations of the National Broadcasting Company network each Saturday at 4 p. m. Eastern War Time (3 p. m. Central War Time, 2 p. m. Mountain War Time and 1 p. m. Pacific War Time). Some stations may record the program and broadcast it at a time which suits their schedule better. Local newspaper radio announcements should be consulted.

Postwar Medical Service

COMMITTEE ON POSTWAR PLANNING

Report of the Subcommittee on Revision of Program for Enrolment of Medical Students

After a careful analysis of present and probable postwar needs for medical service and the supply of physicians available to meet these needs, your subcommittee is convinced a serious shortage of physicians will develop in this country unless there is a continuance of the full complement of medical students. Under existing conditions, this will not be possible. There is no provision for the deferment of suitable qualified applicants in premedicine and medicine subsequent to 1945.

It is estimated that during 1945 about 75 per cent of the normal enrolment of first year medical students can be provided as follows: Army (A. S. T. P.) 28 per cent, Navy (V-12) 25 per cent and physically disqualified for military service (including 4F, returned veterans, aliens and others) and women 22 per cent. At present the only prospects for students during 1946 can come from the following sources: Army none, Navy 10 per cent and physically disqualified and women possibly 30 to 35 per cent. Hence there will be unfilled about two thirds of the places in the freshmen classes of approved medical schools or 1,500 vacancies.

Recently there has been introduced into the Senate by Hon. Mr. Ellender a bill known as S. 637, dated Feb. 25, 1945, that would authorize "the release of persons from active military service and the deferment of persons from military service, in order to aid in making possible the education and training of physicians and dentists to meet essential needs."

Your subcommittee after a careful study of the bill believes it embodies the essential provisions to meet the current defect. It recommends the committee express approval of the general features of the bill and support the bill by means of appropriate action through its constituent organizations and other organizations and individuals interested in the health and medical care of the nation.

ERNEST E. IRONS, M.D. MORRIS FISHBEIN, M.D.
VICTOR JOHNSON, M.D. HAROLD DIEHL, M.D.
HAROLD C. LUETH, M.D.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. Res. 192 has passed the House, authorizing the Committee on World War Veterans' Legislation, acting as a whole or by subcommittee, to conduct an investigation of the Veterans Administration with a particular view to determining the efficiency of the administration and operation of Veterans Administration facilities. H. Res. 204 has passed the House authorizing an appropriation not to exceed $50,000 for the purpose of enabling the Committee on Ways and Means to obtain information with respect to the need for amendment and expansion of the Social Security Act, with particular reference to old age and survivors' insurance, and the problems of coverage, benefits and taxes related thereto. H. Res. 206 has passed the House providing an additional appropriation not to exceed $15,500 to enable the Committee on Labor to continue its investigation of the extent and character of aid now given by the federal, state and local governments and private agencies to the physically handicapped.

Bills Introduced.—S. 759, introduced, by request, by Senator McCarran, Nevada, and H. R. 2710, introduced by Representative Sumners, Texas, would authorize any United States commissioner specially designated for that purpose by the District Court of the United States for the Eastern District of Virginia or by the District Court of Maryland to have jurisdiction and authority to commit to St. Elizabeths Hospital in the District of Columbia, for observation and diagnosis, any person found in any place over which the United States has exclusive or concurrent jurisdiction in Arlington County, Fairfax County or the city of Alexandria, in the state of Virginia, or in Montgomery County or in Prince Georges County, Md., who is alleged and is believed by the commissioner to be of unsound mind. S. 800, introduced by Senator Langer, North Dakota, proposes an appropriation of $20,000,000 for the establishment and operation of a National Infantile Paralysis Clinic at Minneapolis, to include facilities for the hospitalization and treatment of persons suffering from infantile paralysis, and investigation and research with respect to the origin, causes and means of control of that disease. The bill proposes to create a board of five, appointed by the President from among persons who have had infantile paralysis and who have been treated therefor in accordance with the methods "discovered and practiced by Sister Elizabeth Kenny," with authority to take such action as may be necessary to carry out the purposes of the bill. H. R. 2716, introduced by Representative Randolph, West Virginia, provides for health programs for government employees, such programs to be limited to (1) treatment of minor illnesses and dental conditions except in case of an emergency or injury or illness sustained while in the performance of the employee's duty in accordance with the United States Employees' Compensation Act, (2) preemployment and other examinations, (3) referral of employees to private physicians and dentists and (4) education and preventive programs relating to health, including the alleviation of health hazards in the working environment. H. R. 2820, introduced by Representative Maloney, Louisiana, provides that any period of active duty in the United States Revenue Cutter Service during the Spanish-American War, on board the *Galveston* or any other ship of the United States and while such ship was cooperating with the War Department, shall be considered active military or naval service for the purposes of laws administered by the Veterans Administration.

STATE LEGISLATION

Connecticut

Bill Introduced.—H. 1144 proposes to create a board of administrative research and planning to consist of five members appointed by the governor. The board is to collect and compile information, data and statistics, among other things, on health and other factors which may affect the governmental structure and social and economic life of the state.

Georgia

Bills Introduced.—H. Res. 113 and S. Res. 39 propose to commit the state administration to making possible a more intensive health program in the state and to authorize the state board of health to accept on behalf of the state such health funds as may be made available by the federal government.

Illinois

Bill Introduced.—H. 325 proposes to appropriate $4,000,000 to pay $1.50 per day for each patient suffering from tuberculosis to any sanatorium board which provides hospital or sanatorium care under medical supervision at public expense for each such patient hospitalized.

Maryland

Bill Introduced.—Joint Resolution 13 proposes to request the governor to appoint a special commission of nine to study the whole field of medical care and to submit its report and recommendations to the Legislative Council by Sept. 1, 1946 and to the General Assembly in January 1947.

Massachusetts

Bill Introduced.—H. 1738 proposes to enact a separate chiropractic practice act to create an independent board of chiropractice examiners to examine and license applicants for licenses to practice chiropractic. The bill proposes to define chiropractic as "the science of locating, and removing, by hand only, interference with the transmission or expression of nerve force in the human body, and the correction of misalinement or subluxations of the vertebral column. It excludes operative surgery, prescription or use of drugs or medicine or the practice of obstetrics, except that the x-ray may be used solely for the purpose of examinations."

Minnesota

Bill Introduced.—H. 1206 proposes to permit any county or two or more adjacent counties to establish and maintain a county or district health department.

Missouri

Bills Introduced.—H. 250, to amend the osteopathic practice act, proposes to make it unethical conduct, for which a licentiate's license may be revoked, for a licensed osteopath "to fail to designate him or herself as osteopathic physicians or osteopathic surgeons or osteopathic physicians and surgeons." S. 89 proposes so to amend the narcotic drug act as to include isonipecaine within the meaning of the term "narcotic drugs" as used in the act.

New Jersey

Bills Introduced.—A. Con. Res. 16 proposes to direct the director of health to study and report to the next legislature concerning the practicability of the operation by the state of a program to collect, process and distribute human blood and human blood derivatives, including special therapeutic and diagnostic serums deemed of value in the treatment and prevention of certain diseases. A. 381 proposes to direct the department of health to establish, equip, maintain and conduct a suitable program to collect, process, store and distribute human blood and human blood derivatives, including special therapeutic and diagnostic serums, deemed of value in the treatment and prevention of certain diseases. The bill proposes to appropriate $100,000 to the department of health to carry out the provisions of the bill. A. 385 proposes that any hospital exempt from taxation shall likewise be exempt from assessments for public or local improvements.

Oklahoma

Bills Introduced.—H. 386 authorizes the establishment in counties having a population exceeding 175,000 of public health districts coextensive with county boundaries. H. 468 proposes to prohibit the operation of a hospital, sanatorium, rest home, nursing home or related institution, without a license from the state commissioner of health. H. 476 proposes to direct the state commissioner of health to survey the location, size and character of all existing public and private hospitals and health centers within the state and to evaluate the sufficiency of such facilities to supply adequate health services to the people of the state. H. 478 proposes to authorize the state commissioner of health to formulate a state plan for the construction of public and other nonprofit hospitals and other health facilities and to submit the plan to the Surgeon General of the United States Public Health Service for his approval. Any plan approved by the Surgeon General is to be administered by the commissioner of health.

Pennsylvania

Bills Introduced.—S. 544 proposes to prohibit the sale at retail or dispensing of penicillin except on the written prescription of a licensed physician, dentist or veterinarian. S. 579 proposes that every hospital shall require as a prerequisite to the performance of a surgical operation in the hospital that a thorough preoperative study shall have been made prior to the operation. The bill proposes to make it the duty of the operating physician to see that such preoperative study is made and properly recorded among the records of the hospital. The provisions of the bill, however, are not to apply with respect to an emergency operation. H. Res. 19 proposes to direct the public health committee of the senate, the public health and sanitation committee of the house and the secretary of health jointly to formulate an adequate rheumatic fever program for the commonwealth and to submit within thirty days after the passage of this resolution recommendations to the general assembly for the enactment of appropriate measures. H. 1079 proposes to enact a separate massage practice act and to create an independent board of massage to examine and license applicants for license to practice massage. H. 1158 proposes to appropriate $100,000 to the department of health to conduct research to determine the cause, mortality rate, methods of treatment, prevention and cure of cancer and allied diseases. H. 1192 proposes to authorize the governing body of any city, borough, town or township to enter into agreements with private and municipal hospitals serving the community for the payment of the cost of treatment and care of indigent persons affected with contagious diseases requiring hospitalization.

Council on Medical Service and Public Relations

INSURANCE OFFICIAL WARNS AGAINST SHORT CUT TO SECURITY

A warning against a short cut to security was voiced by Mr. James A. Fulton, president of the Life Insurance Association of America in a talk March 14 at a meeting in New York of the Hospital Service Plan Commission and its committees. The commission is a national organization to coordinate activities of the various Blue Cross plans. The Life Insurance Association of America is composed of seventy life insurance companies of the United States.

"They want a short cut, and that short cut is, of course, collective action by government, which always has and always will be the death of liberty and, eventually, the destruction of the very security which it starts out to achieve." Mr. Fulton said, in part, "These are the same people who were saying to us a few years ago that we were far behind the European countries in what they called 'social legislation.' They were spreading out the fact that Germany had had social insurance on a broad scale for many years. Their advocacy has not changed, but I no longer hear them pointing to Germany as an example of what we should attempt here in this country. They seem to overlook the fact that a free people must be a strong people, a self-reliant people, and that self reliance grows with the assumption of individual responsibility and dies with the delegation of the responsibility to the state.

"Life insurance companies and Blue Cross plans are soldiers in a common cause in their efforts to enable American people to achieve security through their own efforts. Our job is to do such a job collectively that there will be no excuse for the government taking over our field."

COMMITTEE ON SOCIAL INSURANCE APPOINTED BY MUTUAL ASSOCIATION

The National Association of Mutual Casualty Companies has appointed a Committee on Social Insurance to improve the handling of physical disability problems such as nonoccupational sickness and accidents for low income groups.

This committee is charged with the responsibility of developing a constructive program which would broaden existing insurance resources to fulfil the need which exists in the nonoccupational field and which is not being met at the present time. The committee feels that as a first step medical, hospital and surgical coverage should be made more generally available by private insurance carriers to meet the growing demand of the public. It is a further objective of the committee to cooperate with the medical profession and industry in working out as far as possible the broader aspects of a program which will fulfil the public need, but in such a way as to develop rather than retard the advantages of private enterprise in the fields of medicine and industry.

The National Association of Mutual Casualty Companies, 919 North Michigan Avenue, Chicago, includes among its members the largest mutual carriers in the casualty field. It is represented on the Conference Committee on Extension of Insurance of the State Medical Society of Wisconsin.

Society Proceedings

COMING MEETINGS

California Medical Association, Los Angeles, May 6-7. Dr. George H. Kress, 450 Sutter Street, San Francisco 8, Secretary.
Rhode Island Medical Society, Providence, May 16-17. Dr. William P. Buffum, 122 Waterman Street, Providence 3, Secretary.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Hitchcock Lectures.—Dr. Franz Weidenreich, honorary director of the Cenozoic Research Laboratory and former professor of anatomy at Peiping Union Medical College, Peking, China, will deliver the second group of Hitchcock Lectures for 1945 at the University of California, Berkeley, during April. The Hitchcock Foundation lectures, of which Dr. Weidenreich will give five on "The Physical Evolution of Man," are public ones on scientific and practical subjects.

Indian Health Official Visits University.—Col. Sohan L. Bhatia, deputy director general of the Indian Medical Service and dean of the Medical School of the University of Bombay, was a recent visitor to the University of California Medical School, San Francisco. According to the *Clip Sheet* of the university Colonel Bhatia was sent by the Indian government to study methods of administration and organization in various medical schools in the United States. He will aid in the initiation of a public health program in India and will help to found a number of medical schools throughout the country.

Memorial to Dr. George Rhodes.—A memorial to the late Lieut. Col. George K. Rhodes, M. R. C., and associate clinical professor of surgery, University of California Medical School, San Francisco, will be established by his friends, patients, former students and associates, according to the University of California *Clip Sheet*. At the time of his death in southern England Colonel Rhodes was the consulting surgeon of the Southern Base Section, U. S. Army. Previously he had organized General Hospital No. 30 as the University of California Medical School Unit, headed its surgical service and remained with it until his appointment as consulting surgeon. Members of this unit, now on active duty overseas, have collected more than $2,000 for the memorial fund (THE JOURNAL, Sept. 30, 1944, p. 317). A committee of ten is in charge of arrangements, with Dr. Francis S. Smyth, dean of the medical school, as honorary chairman and Dr. H. Glenn Bell, associate professor of surgery, chairman. It has not yet been decided what form the memorial will take, but a surgical fellowship for postgraduate study has been recommended.

CONNECTICUT

Vocational Counseling Service.—Dr. Creighton Barker, New Haven, executive secretary of the Connecticut State Medical Society, is the only medical member of the board of eleven directors of the recently incorporated Vocational Counseling Service. The service is a nonprofit community organization to provide professional vocational and educational counseling, particularly designed to aid discharged veterans in finding the proper occupation. According to the state medical journal, if, after a trial period of three years, the service appears practical and important to the community, it is planned to establish a permanent organization. The headquarters for the service are located at 30 Davenport Avenue. At first the new service will function on a part time basis, and currently five experienced counselors of the Yale University faculty have been secured. Individuals will be expected to pay for services rendered at a reasonable cost, but arrangements have been made so that persons with limited means may be able to secure the service if required.

ILLINOIS

Gift to Improve Teaching of Science.—The Francis Shimer College, Mount Carroll, has received a bequest from the late Dr. Blanche M. Haines, Three Rivers, Mich., of $20,000 to set up the George R. Moore Memorial Fund to be used to improve and promote the teaching of sciences. Dr. Haines graduated at the Woman's Medical College, Chicago, in 1886 and the fund honors her father, who died in 1910.

Chicago

Dr. Kretschmer Lectures.—Dr. Herman L. Kretschmer, President of the American Medical Association, addressed the Winnebago County Medical Society, Rockford, March 13, on "Problems in Kidney Surgery" and the Aux Plaines Branch of the Chicago Medical Society, March 23, on "Differential Diagnosis in Renal Disease."

The William Hamlin Wilder Lecture.—Karl Paul Link, Ph.D., professor of biochemistry, Wisconsin Agricultural Experiment Station, Madison, will deliver the second William Hamlin Wilder Memorial Lecture of the Institute of Medicine of Chicago at the Palmer House, May 25. His subject will be "The Anticoagulant Dicumarol."

Hospital News.—Mount Sinai Hospital has established a blood bank under the direction of its pathologist and director of laboratories, Dr. Israel Davidsohn. The bank was established primarily to facilitate the blood transfusion service to patients at Mount Sinai Hospital. As the bank makes progress, it is hoped that blood may be made available in modest amounts to patients outside the hospital.

Dr. Wakerlin Given New Appointment.—Dr. George W. Wakerlin, professor and head of the department of physiology, University of Illinois College of Medicine, has been appointed to serve also as assistant dean in charge of teaching and research at the Rush-Presbyterian Hospital, division of the University of Illinois College of Medicine. Dr. Wakerlin will work with the administration of the hospital, the Rush faculty, and the college of medicine in developing a comprehensive program of undergraduate and graduate medical education and research at Presbyterian Hospital and the Central Free Dispensary. A number of appointments to research positions in the medical sciences are to be made as part of this program.

Gift of $175,000 for Pediatric Research.—A grant of $175,000 to the University of Chicago for research in pediatrics from the estate of the late Dr. Walter H. O. Hoffmann was announced on March 28. The gift brings to $832,722 the amount for support of teaching and research into the care and nurture of children since Dec. 15, 1944, newspapers report. Other gifts to the university include $25,940 from the general education board for verbal tests in I. Q., $20,000 from the Sonia Shankman Foundation for scholarships and research in the university's orthogenic school, two of $15,000 for cancer research from the Albert and Mary Lasker Foundation and the Frances and Sidney Brody charitable fund, $15,000 from Mrs. R. S. Maguire for university support, $10,000 from T. Philip Swift for the department of medicine and $10,000 from the E. J. Brach fund for general research.

The Veteran and His Community.—The University of Chicago opened a public lecture series on the veteran and his community, April 4, with a talk by William T. Hutchinson, Ph.D., chairman of the department of history, University of Chicago, on "The Veterans of Previous Wars." Subsequent lectures will be:

R. W. Marshall, in charge of vocational rehabilitation and education, Chicago Branch Office of Veterans Administration, Legislation Concerning the Veteran, April 11.
C. Edward Thorney, executive director, Veterans Information Center of Metropolitan Chicago, Who is to Deal with the Veteran—and How? April 18.
Dr. David Slight, professor of psychiatry, University of Chicago School of Medicine, Some Psychologic Problems of the Veteran, April 25.
Col. John R. Hall, M. C., commanding officer, Gardiner General Hospital, Health of the Veteran, May 2.
Miss Adeline Johnesse, psychiatric case consultant of Chicago chapter, American Red Cross, Family Adjustment of the Veteran, May 9.
Col. H. H. Weimer, veterans employment representative for Illinois, Veterans Employment Service, Employment of the Veteran, May 16.
Robert K. Burns, chairman of the Daily Newspaper Printing and Publishing Commission, National War Labor Board, What Kind of Jobs Can the Veteran Find? May 23.
Floyd W. Reeves, Ph.D., professor of administration, University of Chicago, Education of the Veteran, June 6.
Lester Benston, director of rehabilitation, American Legion, Community Adjustment of the Veteran, June 13.

INDIANA

Rabies Order in Indiana.—A quarantine for rabies was placed March 23 on Fort Wayne and all Allen County, newspapers reported. The action was taken after at least one mad dog bit at least 6 persons. Three of them on March 22 proved to have received rabies from the bites.

School of Medicine Commended for "Record of Service."—In a report made to the Indiana General Assembly recently by a special legislative investigating committee representing the two houses of the general assembly, the Indiana University School of Medicine, Indianapolis, was given commendation for its "splendid record of service." The inquiry was based on a resolution stating that the Indiana University School of Medicine "has been for some years limiting the number of students" so that "for some years past, even before the war, there was a scarcity of medical doctors in the state." The committee after its inquiry found that "it has been the policy of the Indiana Medical Center not to limit the number

of students entering the school and to graduate as many medical doctors as is possible without lowering the standards of the school and with regard to the facilities available." The committee's report further declared:

That the state of Indiana has not increased the number of medical students graduated in proportion to the increase in population, probably because Indiana has only one medical school compared with some neighboring states which have more than one, and further because the facilities at the Indiana Medical Center have not been expanded within the last ten years or more.

That it would not be expedient at this time to consider enlarging the facilities of the Indiana Medical Center because of the present national emergency and because further the committee has found that the medical school has given to the war 83 members of its staff and further that in all probability there will be a shortage of students within the next few years seeking admission because a large majority of that group is now serving in the armed forces of the United States.

KANSAS

Clendening Gift for Medical History.—The University of Kansas Endowment Association has received a $50,000 bequest under the will of the late Dr. Logan Clendening, Kansas City, Mo., to be used for the department of medical history. It is the understanding of Dr. Harry R. Wahl, Kansas City, dean of the medical school, that Dr. Clendening wished the money used to maintain the library of medical history, according to the state medical journal.

Personal.—Dr. Chester D. Updegraff, Greensburg, was recently elected coroner of Kiowa County.——Dr. Albert N. Gray, Burlington, was reelected coroner of Coffey County. ——Dr. George Seitz, Salina, has been appointed Saline County health officer, succeeding Dr. Edwin G. Ganoung, Salina.

Postgraduate Medical Clinic on Poliomyelitis.—Dr. Edward A. Piszczek, director of the Cook County Public Health Unit, Chicago, and Gustav Valdemar, director of physical therapy, Children's Hospital, Denver, conducted a postgraduate medical clinic on poliomyelitis March 17-25 under the auspices of the Kansas Medical Society, the state board of health and the University of Kansas School of Medicine, Lawrence-Kansas City. The course was conducted two days each in Kansas City, Parsons, Salina, Wichita and Topeka. The general topics of basic knowledge of infantile paralysis, diagnosis of poliomyelitis and treatment were discussed from medical and physical therapeutic aspects. The speakers were furnished at the request of the state board of health by the National Foundation for Infantile Paralysis.

MAINE

Medical Examiners Appointed.—Governor Hildreth has appointed the following medical examiners for four year terms each:

Androsoggin County: Drs. Romeo A. Beliveau, Lewiston, and Harold S. Pratt, Livermore Falls.
Aroostook County: Drs. Francis J. Faucher, Grand Isle; Frank H. Jackson, Houlton, and Herrick C. Kimball, Fort Fairfield.
Cumberland County: Drs. John M. Bischoffberger, Naples; Ervin A. Center, Standish, and William Holt, Portland.
Franklin County: Dr. George L. Pratt, Farmington.
Hancock County: Drs. Charles C. Knowlton, Ellsworth; George A. Gregory, Boothbay Harbor, and Joseph E. Odiorne, Whitefield.
Kennebec County: Drs. Roland L. McKay, Augusta; Leon D. Herring, Winthrop; John G. Towne, Waterville, and Clarence R. McLaughlin, Gardiner.
Oxford County: Drs. Kenneth E. Dore, Fryeburg; John A. Greene, Rumford, and Delbert M. Stewart, South Paris.
Penobscot County: Drs. Herbert C. Scribner, Bangor; Cornelius J. Taylor, Bangor; Herbert Lewis Taylor, Dexter; G. Frank Woodbury, Patten, and Ernest T. Young, Millinocket.
Piscataquis County: Dr. Albert M. Carde, Milo.
Sagadahoc County: Dr. Edwin F. Pratt, Richmond.
Somerset County: Dr. Walter S. Stinchfield, Skowhegan.
Waldo County: Drs. Edward P. Goodrich, Winterport, and Orris S. Vickery, Belfast.
Washington County: Drs. James C. Bates, Calais, and Oscar F. Larson, Machias.
York County: Drs. George R. Love, Saco; James H. Macdonald, Kennebunk, and Paul Taylor, Kittery.

MARYLAND

Changes in Health Officers.—Dr. Theodore R. Shrop, Oakland, recently resigned as deputy state and county health officer of Garrett County. Dr. Louis G. Llewelyn, Pokomoke City, resigned a similar position in Worcester County.

Hospital Ward for Premature Babies.—Plans are under way to establish a new ward at the Harriet Lane Home for Invalid Children, Johns Hopkins Hospital, Baltimore, to provide special care for premature babies. The proposed unit will accommodate 24 babies and the project is being financed in part by the federal government.

Rapid Treatment Center in Baltimore.—A rapid treatment center of 60 beds for patients with venereal diseases was opened at the Baltimore City Hospitals recently with the aid of medical and nursing personnel furnished by the U. S. Public Health Service. The treatment center was opened primarily for the purpose of assisting the city health department venereal disease clinics and other related medical agencies in the prompt and isolated treatment of cases of disease in the infectious stage. The health department bureau of venereal diseases is acting for the city welfare department as the admission service for these specialized hospital beds.

MISSOURI

Community Award Goes to Blue Cross Plan.—On April 5 the annual Community Service Award for 1945 of the Hospital Council of Saint Louis will be presented to the St. Louis Blue Cross Plan. The award is given each year to the organization or individual making the greatest contribution to the community's health.

Lectureship in Honor of Hanau W. Loeb.—The Alpha Pi chapter of Phi Delta Epsilon has created a lectureship in honor of the late Dr. Hanau W. Loeb, formerly dean of the St. Louis University School of Medicine. The presentation of the lectureship to the school of medicine will take place at a dinner meeting at the Coronado Hotel, April 9, by Dr. Arthur E. Strauss, St. Louis, past grand consul of the national organization of Phi Delta Epsilon, on behalf of the fraternity. All interested persons are cordially invited to attend the dinner, reservations for which may be made by communicating with the dean, Rev. Alphonse S. Schwitalla, S.J., of St. Louis University School of Medicine, 1402 South Grand Boulevard, St. Louis 4.

NEW YORK

Nelson Russell Honored.—The Chancellor's Medal of the University of Buffalo was presented to Dr. Nelson Gorham Russell, Buffalo, February 22, inscribed "in recognition of a lifetime of eminent service to your profession, your community and your country which has 'dignified Buffalo in the eyes of the world'." Dr. Russell, who has been associated with the University of Buffalo School of Medicine for fifty-three years, was also cited as a "scientist, soldier, civic leader, teacher and mentor of two generations of physicians and dean of the practitioners of the healing art in this region." Dr. Russell graduated at Buffalo in 1895, joined the faculty as instructor in general pathology about 1897 and is now emeritus professor of medicine.

Cancer Symposium.—On April 13 the Nassau County Cancer Committee, in cooperation with the Nassau County Medical Society, will present an all day cancer symposium for physicians at the Garden City Hotel, Garden City. Among the speakers will be:

Dr. Earle G. Brown, Mineola, Five Years of Cancer Reporting in Nassau.
Dr. Lloyd F. Craver, New York, Diagnostic Problems of Early Cancer.
Dr. Clyde L. Deming, New Haven, Conn., Cancer of the Genito-urinary Tract.
Dr. James A. Corscaden, New York, Gynecologic Cancer.
Edith H. Quimby, Sc.D., New York, Physical Basis for the Use of X-Rays and Radium in the Treatment of Cancer.
Lieut. Comdr. Charles F. Geschickter (MC), Cancer of the Breast.
Dr. George T. Pack, New York, Gastrointestinal Cancer.

Bill Passed to Open All Medical Graduates for Licenses to Practice Medicine.—A bill has been passed in both houses of the assembly in New York directing the state medical examiners to admit up to July 1, 1946 to examination any candidate "who shall have satisfactorily completed a four year course, consisting of at least eight months a year, in any medical school in this country." The bill has been sent to the governor for signature. The New York *Times* reported that final approval was given in the senate, where the measure, sponsored by Assemblyman Wheeler Milmoe, Canastota, was passed by a vote of 34 to 15 over objections that it would open the door for practice to "pseudo-quacks" who had not attended schools approved by the state board of regents. Elmer F. Quinn, New York, senate minority leader, spoke for the bill, declaring that the only group opposing the measure was the state medical society. He asserted that many hospitals in New York City were forced to depend largely on interns to attend the sick and that these interns could not be licensed because the schools they attended were not approved by the state.

Irvington House and New York University College of Medicine Now Affiliated.—The New York University College of Medicine, New York, and Irvington House, sanatorium for cardiac children, Irvington, have established a medical affiliation to further the care and rehabilitation of underprivileged children with heart disease. Under the terms of the affiliation the college of medicine of the university will be responsible for the direction, supervision and administration of the medical and research program at Irvington House, the

announcement stated. The sanatorium will be used as a teaching center to train young doctors in the early recognition and treatment of rheumatic heart disease. While the New York University College of Medicine, under the terms of the affiliation, will have full medical responsibility for the direction of the institution, Irvington House will continue to depend on an annual appeal for voluntary contributions for its financial support. One of the major results expected from the new affiliation, according to Dr. Donal Sheehan, acting dean of the college of medicine, is an expansion of the sanatorium's research activities in the cause, prevention and treatment of rheumatic fever. In the past three years, promising studies in the prophylactic use of sulfonamide drugs have been conducted at Irvington House, and that type of work will be continued. Since its establishment twenty-five years ago, Irvington House has provided free care for more than 3,000 underprivileged children referred to it by about forty hospitals of greater New York and Westchester, and the present building, erected under the supervision of the New York Heart Association, contains an entire floor devoted to laboratories. Dormitories, school rooms, a dental clinic and recreation and craft workshops accommodate more than 100 children for periods ranging from six months to several years. It conducts a demonstration in rehabilitation and medical research of benefit to children throughout the country.

New York City

Eighteenth Graduate Fortnight. — "Contributions of the War Effort to Medicine" will be the theme of the eighteenth graduate fortnight of the New York Academy of Medicine, October 8-19.

The Harvey Lecture.—William F. Windle, Ph.D., professor of neurology, Northwestern University Medical School, Chicago, will deliver the seventh Harvey Society Lecture of the current series at the New York Academy of Medicine, April 19. His subject will be "Respiratory Conditions in the Fetus and Effects of Their Impairment."

The Miller Memorial Lecture.—The Adam M. Miller Memorial Lecture of the Long Island College of Medicine, Brooklyn, will be delivered by Edmund V. Cowdry, Ph.D., professor of anatomy, Washington University School of Medicine, St. Louis, April 23. Dr. Cowdry will speak on "Microscopic and Chemical Properties of Precancerous Lesions."

Commercial Stores Cooperate with Health Department in Tuberculosis Drive.—By means of window displays, newspaper advertisements, posters and other devices, retail stores will cooperate with the New York City Department of Health in a campaign against tuberculosis during April. The objective will be to urge the public to have chest x-rays. The campaign is being supported by the Fifth Avenue Association, the Retail Dry Goods Association and the Uptown Retail Guild. A release states that persons dialing the telephone number for a weather report will also hear a reminder at the end of the forecast to have a chest x-ray.

Howard Blakeslee Honored. — Howard W. Blakeslee, science editor for the Associated Press since 1928 and member and former president of the National Association of Science Writers, was guest of honor at a dinner at the Waldorf-Astoria Hotel, March 21, in recognition of his sixty-fifth birthday and the completion of forty years of service with the Associated Press, which he has served in various capacities since 1905. Representatives from colleges and universities, industrial research laboratories, the medical profession and the press were among those at the dinner. Speakers included Charles E. Honce, assistant general manager of the Associated Press; Robert C. Hockett, Ph.D., Cambridge, Mass., scientific director of the Sugar Research Foundation, and Mr. Blakeslee. The University of Michigan, Ann Arbor, which Mr. Blakeslee attended, awarded him the honorary degree of master of science in 1935. He shared the Pulitzer Prize in 1937 and received the award of the National Headliners Club in 1940.

Proposed Medical Center.—The construction of a giant medical center, part of the plans for which had been previously announced, to be undertaken cooperatively by New York City and New York University in the Bellevue Hospital area, will begin as soon as materials are available, according to Mayor Fiorello H. La Guardia in the New York *Times*, March 19. The mayor is said to have estimated the cost of creating the new medical center at $27,500,000, of which $12,500,000 would be the city's share. Harry Woodburn Chase, LL.D., chancellor of New York University, announced at the same time that the university would make a public appeal to raise its $15,000,000. It was stated that most of the Bellevue Hospital buildings would be razed to make room for the new hospital. In a statement the mayor said "We're going to rebuild Bellevue Hospital entirely. It is cheaper to build a new hospital than to remodel. We will reconstruct all the facilities at Bellevue except the diagnostic and will retain the new administration building and psychopathic department." The new building for Bellevue Hospital will have accommodations for at least 2,300 beds. New York University College of Medicine is now said to be preparing a prospectus for a new school and hospital for 450 beds on a site from East Thirtieth Street, north of Bellevue, at East Thirty-Third Street between First Avenue and East River Drive. The new hospital and center would provide flexibility in the clinical distribution of patients and for adjustments under the Health Insurance Plan of Greater New York, Inc., it was stated. An institute for forensic medicine will be a part of the center under an agreement by which the university will give the land to the city and the city will construct the building (THE JOURNAL, June 26, 1943, p. 630). Plans call for a new and enlarged department of preventive medicine in the medical college building to aid clinics now established on the lower east side. One half of the $15,000,000 proposed as the university's share in the new construction will be spent for new buildings and the other half will be used as endowment. Two other units under consideration would be a small semiprivate hospital and an institute of medical sciences, which would offer research laboratories to younger men for study in specially important fields. The hospital would offer all methods of modern diagnosis, together with inpatient facilities, to families of the middle-low income group, based on the needs of persons subscribing to the Health Insurance Plan.

PENNSYLVANIA

Society News.—Dr. Charles C. Wolferth, Philadelphia, will address the Delaware County Medical Society at the Chester Hospital, Chester, April 12, on "Recent Advances in the Treatment of Cardiovascular Diseases."

Accidents to Physicians.—Dr. William D. Schrack Jr., Harrisburg, bureau of health conservation of the state health department, suffered severe injuries when his automobile collided with a Greyhound bus near Sunbury while negotiating a narrow pass through snow drifts, according to the *Pennsylvania Medical Journal*. Dr. J. Fletcher Lutz, York, was badly injured while taking a patient to the hospital; he alighted to clean ice from his windshield, when a truck crashed into his automobile.

Meeting on the Eye and Ear Canceled.—The proposed spring meeting of the newly formed Pennsylvania Academy of Ophthalmology and Otolaryngology, scheduled for April 25-26 at the Merion Golf Club, Ardmore, has been canceled. The academy was formed in 1944 from a reorganization of the Eastern Pennsylvania Association of Eye, Ear, Nose and Throat Physicians, the latter group having been created at a meeting in Pottsville in 1942. Dr. Sterling F. Mengel, Pottsville, the first secretary of the Eastern Pennsylvania group, on active duty with the Navy, was named secretary of the academy. Dr. Paul C. Craig, Reading, is now serving as acting secretary.

Philadelphia

Rheumatic Fever Made a Reportable Disease.—Effective immediately, rheumatic fever and rheumatic heart disease are reportable to the division of communicable disease of the department of public health. According to *Philadelphia Medicine*, all physicians are requested to cooperate in this matter.

Postgraduate Institute Postponed. — The tenth annual postgraduate institute of the Philadelphia County Medical Society, scheduled to be held at the Bellevue-Stratford Hotel, April 10-13, has been postponed as the result of the request of the government for the curtailment of all nonessential meetings, according to the *Pittsburgh Medical Bulletin*.

RHODE ISLAND

Medical Aspects of Air Pollution.—On April 2 Dr. Clarence A. Mills, professor of experimental medicine, University of Cincinnati College of Medicine, discussed the medical aspects of air pollution at a meeting of the Providence Medical Association. The talk was a part of the program of the committee on air pollution of the association, which is preparing a schedule of study and action in the hope of improving the air in Providence.

Voluntary Hospitalization Insurance Accepted for Another Year.—On February 19 the Rhode Island Voluntary Advisory Council on Health approved a recommendation of its technical committee that the principle of voluntary hospitalization insurance be accepted for another year. The voluntary advisory council was appointed by Governor J. Howard McGrath in 1944. At its first meeting, Feb. 5, 1944, it created its technical committee for the study of hospital insurance and

related problems, which subsequently divided itself into two divisions, one studying a proposal for medical and surgical benefits and the other concentrating on the proposal for compulsory hospital insurance. The technical committee, cognizant that the house of delegates of the state medical society has appointed a committee to study the possibility of providing surgical care on a prepaid basis, recommends that this group continue its study and make its report public. The committee endorses the principle of prepaid hospital cost through insurance and recommends employers, employees and the general public to participate voluntarily in order that there may be as widespread protection as possible. The *Rhode Island Medical Journal* states that by deferring action on a plan of compulsory insurance until the next annual session of the general assembly a period of time would be available during which employers and employees would become better acquainted with the advantages of hospital insurance and make such arrangements as they might desire to secure such coverage. As hospital facilities are not now available to care for their number of patients that might be expected if compulsory insurance were made effective immediately and cannot be provided until postwar conditions make building on a large scale possible, relatively little would be lost and much gained by using the intervening time to enroll as many persons as possible under a voluntary method.

TENNESSEE

Edwin Reinke Dies.—Edwin Eustace Reinke, Ph.D., associated with the department of biology of Vanderbilt University, Nashville, since 1915 and chairman of the division of natural sciences and mathematics since 1941, died at Vanderbilt University Hospital, January 25.

ALASKA

Personal.—Dr. William M. Whitehead, Juneau, has been appointed to the Territorial Board of Education for a term of six years.

Dr. Carter Named Commissioner of Health.—Dr. Cassius C. Carter, Juneau, who has been serving as commissioner of health since the death of Dr. Walter W. Council, Nov. 13, 1943, has now been appointed by the governor for the remainder of the term.

GENERAL

Charles Stephenson Named Secretary of Research for Cancer Society.—Rear Admiral Charles S. Stephenson (MC), U. S. Navy, has been appointed secretary of the research division of the American Cancer Society. Through his department will be cleared all inquiries and requests for aid received as a result of the announcement that a large portion of this year's campaign funds will be definitely earmarked for research.

Actions on 1945 Conventions.—Reports received by the American Medical Association indicate the following action for the 1945 sessions of the respective organizations:

American College of Chest Physicians June meeting in Philadelphia canceled; the business meeting of the board of regents will be held in Chicago, June 17.
Medical Society of New Jersey, canceled.
American Student Health Association, canceled.

Brochure on Borden Awards.—The Borden Company has published a directory of recipients of Borden Awards distributed through the American Chemical Society, the American Dairy Science Association, American Home Economics Association, American Institute of Nutrition, American Academy of Pediatrics, Poultry Science Association and American Veterinary Medical Association. In addition to indicating the year and the winner for each of the awards, the biography of the 1944 recipients has been included.

State and Territorial Health Officers to Hold Meeting.—The forty-third annual conference of the U. S. Public Health Service with the state and territorial health officers will be held April 9-11 in the National Academy of Sciences, 2101 Constitution Avenue, Washington, D. C., according to *Public Health Reports*. All state health officials are urged to attend. The meeting is required by law and therefore has been approved by the committee on conventions. General sessions of the conference are open to all interested persons but attendance by out-of-town visitors is not encouraged in view of travel restrictions.

Postage Meters Used in Cancer Campaign Appeal.—The American Cancer Society this year has enlisted the cooperation of the Pitney-Bowes Postage Meter Company, Stamford, Conn., in preparing a design which they are offering in a mailing addressed to all of their customers. This mailing has already gone forward. The circular also includes a similar item which Pitney-Bowes is offering in behalf of the American Red Cross drive. Reports from many parts of the country indicate that favorable responses are beginning to come in from local firms. Cooperation is carried out by business houses using these postage meters instead of postage stamps. These meters allow for an advertising message, commonly called a postmark ad.

Father Schwitalla Named Moderator of Physicians' Guilds.—Rev. Alphonse M. Schwitalla, S.J., president of the Catholic Hospital Association and dean of the St. Louis University School of Medicine, St. Louis, has been named moderator of the Federation of Catholic Physicians' Guilds and editor of the federation's journal, the *Linacre Quarterly*. Mr. M. R. Kneifl, St. Louis, executive secretary of the Catholic Hospital Association, has been named acting executive secretary of the federation. The announcement of the change in officers was made March 24 following a meeting of the executive board of the federation at the Hotel Pennsylvania, New York. It was also announced that the federation is now an affiliate association of the National Catholic Welfare Conference. By agreement with the Catholic Hospital Association, the offices of the federation are moved for the present from Brooklyn to the association's offices at 1402 South Grand Boulevard, St. Louis 4. In the business management and administration of the federation, the Catholic Hospital Association will act as agent on behalf of the Catholic Physicians' Guild.

Sigma Xi Lectures on Cancer.—Dr. Peyton Rous, member, Rockefeller Institute for Medical Research, New York, opened a series of lectures on cancer that he will deliver throughout the country March 30 at the University of Virginia, Charlottesville. He spoke April 2 at the North Carolina State College of Agriculture and Engineering, Raleigh, April 5 at Louisiana State University, New Orleans, and April 9 at the University of California, Los Angeles. He will also speak at the following schools:

University of Oregon Medical School, Portland, April 13.
University of Idaho, Moscow, April 17.
Montana State College, Bozeman, April 20.
Mayo Clinic, Rochester, Minn., April 23.
University of Minnesota, Minneapolis, April 24.
University of Wisconsin, Madison, April 25.
University of Chicago, Chicago, April 26.
Washington University, St. Louis, April 27.
Ohio State University, Columbus, April 30.
Virginia Polytechnic Institute, Blacksburg, May 1.
West Virginia University, Morgantown, May 3.
Pennsylvania State College, State College, May 4.
Bucknell University, Lewisburg, Pa., May 7.
Swarthmore College, Swarthmore, Pa., May 8.
Temple University, Philadelphia, May 9.

Nutrition Grants.—Grants totaling $914,190 have been allocated by the Nutrition Foundation since its organization March 12, 1942, according to an announcement March 28. These grants for 100 correlated research projects to increase basic knowledge in the field of nutrition were made to 44 universities and medical centers in the United States and Canada. At the third anniversary meeting of the Nutrition Foundation at the Waldorf-Astoria, New York, March 28, grants totaling $258,100 were approved covering six new research projects and 24 renewals of grants for studies now under way. Among the new grants were the following:

Harvard University received $47,500 for a five year study of nutrition in relation to maternal health, which will include the problems of pregnancy, childbirth, the condition of the newborn infant, and its subsequent health and development.

The Public Health Research Institute of the City of New York received $10,500 for a three year study of the development of microchemical methods for evaluating nutritional status. There is a critical need for practical methods of measuring the influence of nutrition on public health in the marginal zones of malnutrition.

The University of Rochester School of Medicine and Dentistry, Rochester, N. Y., received $10,000, for a two year study of the nature and significance of a pigment associated with vitamin deficiency.

Other grants were made to the University of Pittsburgh for studies on self selection of diets, to Washington University for studies on the mechanism of carbohydrate reactions in animal tissues, and to the University of Wisconsin to study the characterization of compounds containing bound biotin and other vitamins.

CORRECTION

Injuries of the Cervical Spine.—In the article by Dr. Arthur G. Davis in THE JOURNAL, January 20, page 149, incorrect figure numbers appear in two or three places; i. e., on page 150, fourth line of second column, "fig. 5" should read "fig. 3"; page 152, last line of text in first column, "Figure 4" should read "Figure 7," and in the first line of the second column, "Figure 7" should read "Figure 6."

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 7, 1945.

The Uses and Limitations of Penicillin

Sir Alexander Fleming, the discoverer of penicillin, opened a discussion on its uses and limitations before the Medical Society of London. He stated that an important fact about penicillin was that it was not toxic to leukocytes. Ordinary antiseptics, such as carbolic acid, killed the leukocytes more readily than they killed the bacteria. Penicillin was reputed to be bacteriostatic, but it was being established that it was bactericidal as well. It must be brought into contact with the bacteria to be effective. He said that intravenous administration must be repeated because the kidney excretes penicillin very rapidly. With the standard intravenous dose of 15,000 units, most of the penicillin had disappeared from the blood within an hour. With intramuscular injection it remained for about two hours; if 50,000 units was given, for rather more than four hours; if 100,000, rather more than six hours. The intravenous drip was the most economical method but involved certain difficulties; with the intramuscular drip there was a limit to the amount of fluid which could be administered with comfort to the patient. But the subcutaneous drip served the purpose quite well. The latest apparatus for introducing the requisite amount of fluid had a small clock or motor which every hour turns a screw connected with the piston of a syringe, so that up to a million units (about ten times the ordinary dose) could be given subcutaneously in twenty-four hours without discomfort. He stated that the standard dose of penicillin was 124,000 units in twenty-four hours, given either by single injection or by drip. Fleming's clinic had been successfully using half that dose for ordinary organisms, such as the staphylococcus and the streptococcus. For less sensitive organisms the dose has been larger.

Cases of staphylococcic septicemia, Sir Alexander continued, formerly regarded as almost hopeless, invariably recovered. Gonococcic infection seemed the easiest of all to treat. The routine treatment was 100,000 units split into eight or ten doses given at two or three hour intervals. This seemed to cure about 97 per cent of the cases. Such frequent doses were not as suitable for civilians as for men in the services. The plan was often 100,000 units in the morning and 50,000 at night. Syphilis was now being placed on the list of diseases to be treated by penicillin. A start was made with 120,000 units for a week in the usual split doses. This had been doubled, but even with the smaller dosage the spirochetes disappeared in twelve to fifteen hours. The Wassermann reaction became negative, and the patient appeared well, though in some cases there was a relapse. Penicillin was likely to be extremely successful in the mouth and respiratory tract. Nearly all the bacteria common in these regions were sensitive to penicillin; the only difficulty was to get the penicillin into contact with them. Two serious limitations of penicillin were its instability and rapid excretion. Made up in the form of solutions, ointments, creams or lozenges it was unstable. Some would say that it was a disadvantage that it could not be given by the mouth, the acid of the stomach destroying it, but that might be an advantage in preventing its abuse. Great care had to be exercised in making it up, to assure that it is bacteriologically sterile.

In reply to questions Fleming stated that skin irritation did not often follow penicillin therapy and was never serious. The Americans had made claims for penicillin in endocarditis, but he had not much faith in short term treatment. The penicillin had to diffuse into the vegetations and it was necessary to maintain a certain concentration in the blood for a considerable period of time. As to the treatment of tertiary syphilis, he must refer the questioner to American journals, for we had no experience of it in this country.

Government Inquiry on Remuneration of Physicians

Evidently in view of the proposed National Health Service, the minister of health and the secretary of state for Scotland have appointed a committee, of which about half of the members are general practitioners, to consider what ought to be the range of total professional income of a registered medical practitioner in any publicly organized service of general medical practice. This income is to be established with regard to what has been the normal financial expectations of general medical practice in the past, with regard to the desirability of maintaining in the future the proper social and economic status of general medical practice and with regard to its power to attract a suitable type of recruit to the profession. The practitioners on the committee have all been nominated by the British Medical Association, and one of the joint secretaries of the committee is Dr. Violet Kelynack, assistant secretary of the British Medical Association.

Exhibition of War Injuries

After the destruction by German bombs in 1941 of the Army Medical War Collection housed in the Museum of the Royal College of Surgeons, the Medical Research Council was asked by the War Office and the college to assist in forming a comprehensive national collection of specimens, photographs and drawings of war injuries, which would serve both for teaching purposes and as a permanent record of the types of injuries in the present war. A special subcommittee of the war wounds committee of the council was appointed to direct the scheme. This subcommittee includes nominees of the three services, the Ministry of Health, the Department of Health for Scotland, the Royal Colleges of Physicians and Surgeons and the Ministry of Pensions. The arrangements for the collection were entrusted to Dr. Joan M. Ross, who is acting as temporary curator.

The Operative Treatment of Chronic Cerebral Hematoma

In the *British Medical Journal* (February 3, p. 146) Mr. G. F. Rowbotham and Dr. A. G. Ogilvie have described an important advance in cerebral surgery—the operative treatment of chronic cerebral hematomas. The cerebral blood vessels when weakened by disease or congenital malformation may give way under normal strain, producing spontaneous subarachnoid hemorrhage. The clinical picture is usually characteristic. A previously healthy young or middle aged person is struck with sudden severe pain in the head, which radiates into the neck and may reach the fingers and toes. Consciousness may be impaired. Cranial nerve and limb palsies may develop. Blood is always present in the cerebrospinal fluid, so that the diagnosis can readily be made by lumbar puncture. Such hemorrhage may result from rupture of congenital aneurysms of the circle of Willis. Since the aneurysms lie in the subarachnoid space, it is thought that the hemorrhage is always subarachnoid. But occasionally a congenital aneurysm becomes attached to brain tissue and ruptures intracerebrally, to produce a chronic hematoma. Two cases are reported—in a woman aged 28 and a man aged 23—who presented the symptoms of subarachnoid hemorrhage and in whom left hemiplegia and papilledema developed. Under local analgesia a temporal exposure was made. The brain was found to be bulging and obviously under pressure. By means of a brain cannula a cyst 4 cm. in diameter containing altered black blood was found at a depth of 2 cm. The cyst was opened by an incision into the brain tissue and its contents were removed by gentle suction. Recovery followed and both patients regained

health. Rowbotham and Ogilvie describe the operation as a new and successful venture in the therapy of cerebral hemorrhage. They chose to operate at the stage of chronic subdural hematoma and not at the stage of acute cerebral hemorrhage. Possibly in those cases of hemiplegia following a subarachnoid hemorrhage it is also wise to operate even when there is no secondary rise in intracranial pressure. It is noteworthy that the writers doubt whether surgery has much to offer in ordinary apoplexy or, in fact, in the early stages of cerebral hemorrhage due to any cause.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, Jan. 30, 1945.

Vital Statistics of Rio de Janeiro for 1944

Provisional data of vital statistics for the city of Rio de Janeiro for the year 1944 are now available. The population of the city computed as of July 1, 1944 was 1,940,000. The total number of deaths from all causes was 35,907, giving an annual crude death rate of 18.50 per thousand of population. Practically there had been no change in the death rate during the twelve year period 1932-1943, as this rate varied slightly from the average of 17.50 per thousand after a constant and regular decline since the beginning of the century. The number of live births registered in 1944 was 42,583, corresponding to the annual birth rate of 21.95 per thousand of population. With 3,159 stillbirths, the fetal mortality was 69.06 per thousand total births, a figure showing almost no change during the last few years. This is interpreted by Brazilian public health workers as a result of the high prevalence of syphilis in the population. The number of deaths from causes related to pregnancy, childbirth and the puerperium was 283, corresponding to a maternal death rate of 6.65 deaths per thousand live births, or 1 death in 150 live births.

One of the most important causes of death was tuberculosis, with a total of 6,318 deaths (5,996 from tuberculosis of the respiratory system). This is 17.59 per cent of the total number of deaths from all causes.

Brazilian Menthol to the United States

Brazil is now the largest source of crystallized menthol imported by the United States. Since the beginning of the war the culture of Mentha piperita and the extraction of peppermint oil began to develop in São Paulo, Paraná, and the other southern states of Brazil. Yielding 75 to 80 per cent of menthol, the Brazilian variety of Mentha is not as good as that cultivated in Japan, which yielded an average of 85 per cent. It is better than the American variety, which produces an average of only 55 per cent of menthol. During the year 1943 Brazil produced about 50 tons of peppermint oil, from which 20 tons of crystallized menthol has been extracted and sent to the United States. The 1944 production was expected to reach the figure of 300 tons of crystallized menthol, which is about a third of the United States consumption.

Accidents from Venomous Snakes

After India, Brazil is the country most afflicted by the scourge of bites from venomous snakes. There are two great laboratories for the preparation of antivenin serums—the Instituto Butantan and the Instituto Vital Brazil, both founded by Dr. Vital Brazil, in 1901 and in 1920 respectively. Dr. Ruy D. Barroso, from the latter institute, has recently published a study of 2,238 cases of snake bites treated with serum, including men, women, children and pet animals, mostly dogs. The serum most frequently used is prepared with a mixture of venoms from several species of snakes. The cases are distributed as follows: men 62.2 per cent, children 15.0 per cent, women 12.8 per cent and animals 10.0 per cent. The high percentage of men is obviously explained by greater exposure, principally in agricultural work. In 91 of the cases treated, or 4.1 per cent, the victims died, because of too long delay between the bite and the injection of serum, or because an insufficient amount of serum had been used. The fatality rates were 2.6 per cent for men, 3.3 per cent for women, 4.6 per cent for children and 12.9 per cent for animals. From these figures Dr. Barroso concludes that the fatality rate decreases as the weight of the victim increases. The amount of serum must be increased with the lower weight of the victim. Of the total 2,238 cases, 1,271 victims have been hit during the warmer season against 43.1 per cent during the cooler season. The fatality rate (4.1 per cent) varied according to the kind of snake which caused the accident: 2.2 per cent of the cases of Bothrops biting were fatal against 13.2 of the cases of Crotalus biting and 5.4 of the cases of undetermined species. Dr. Barroso believes that anticrotalus serum was less effective and that the amount of antigenic material in the preparation of such a serum should be increased in order to make it much more active.

The Pathologic Picture of Dysentery Caused by Shigella Alcalescens Andrewes

Little has yet been written about the pathologic picture of the dysentery caused by Shigella alcalescens Andrewes, mainly because of the low fatality rate of the disease as compared to the classic dysentery caused by the Shiga and Flexner strains. Thus it is interesting to point out the main features of a fatal case carefully studied and reported by Dr. Arlindo de Assis. The patient was a 16 month old infant who died five days after his admission to the Arthur Bernardes Children's Hospital of Rio de Janeiro. A normal strain of S. alcalescens (serologic type I Assis), without any relationship to the Flexner, the Sonne and the Newcastle-Boyd 88 strains, was recovered from the feces during life and from the colon mucosa after death. Blood from the heart also yielded a prompt growth of the same micro-organism, while the gallbladder content proved to be sterile. Diffuse inflammatory changes were found in a moderate degree in the mucosa of the pelvic colon, occurring along with a rather slight reaction of the local lymphoid tissue. Peyer's patches remained unchanged. The abdominal lymph nodes were apparently normal. A diffuse exudate and inflammatory changes were again observed at the surface of the parietal endocardium (left ventricle) in association with infiltration of mononucleated cells. According to Dr. de Assis the features of the case bring a practical and definitive confirmation of the pathogenicity of Shigella alcalescens Andrewes for man.

Deaths of Dr. Salles Guerra and Dr. Astrogildo Machado

Dr. Egydio Salles Guerra, a retired physician who was a leading surgeon in Rio de Janeiro during the first quarter of the present century, has died at the age of 75. He published several scientific papers and medical books as well as some literary works, including a biographic study of Dr. Oswaldo Cruz. At the inauguration of President Rodrigues Alves in 1902 Dr. Salles Guerra was invited to be director general of the National Department of Health, but he suggested for the post a young and unknown physician, Dr. Oswaldo Cruz, just arrived from Paris, where he had had special training in bacteriology and in parasitology at the Pasteur Institute. Dr. Oswaldo Cruz was appointed and began his successful campaign against yellow fever, freeing Rio de Janeiro of that dreadful scourge and becoming himself a Brazilian medical hero.

Dr. Astrogildo Machado, head of the Division of Bacteriology of the Instituto Oswaldo Cruz, has died at the age of 61. As an assistant of Dr. Carlos Chagas, Dr. Machado contributed to the experimental study of the American trypanosomiasis and developed, in cooperation with Dr. Guerreiro, the serologic diagnostic test for the disease known as the Machado-Guerreiro test.

PARIS

(From Our Regular Correspondent)

Feb. 18, 1945.

A Regimen of Famine and Its Consequences

France has been subjected for the past five years, and is still being subjected, to a dietary regimen of which history has few examples. The Académie de médecine and other scientific societies, as represented by the opinions of Charles Richet (who has been deported to Germany because of his courageous declarations), Lesné, Georges Duhamel, Robert Debré and Mme. Randouin, have constantly protested that the rationing was barbaric. The regimen is not only deficient but poorly balanced. Moreover, the rations are not always properly distributed. Even when the tickets are honored, the average caloric value of the ration never reaches 1,400 calories per day, in the place of 2,400 calories, which are considered as a minimum, and in the place of 3,000 to 4,000 calories, which were customary for the French before the invasion. The ration is made up of 63 per cent carbohydrates, 17 per cent fats and 15 per cent proteins, of which one third is of animal origin. The bread is deficient in nitrogen and is reinforced by an excess of indigestible cellulose. The amount of animal proteins is insufficient in relation to the vegetable proteins; the ration also lacks the proper amount of metallic salts and vitamins.

The ration for nurslings perhaps could be considered satisfactory, but it is also poorly balanced. Infants above the first year and adolescents are the most frequent victims. As of January 1944 children from 3 to 6 years of age instead of receiving a ration equaling that of adults because of the demands of growth did not receive more than 1,321 calories; there were 39 Gm. of fats in place of 80, 29 Gm. of nitrogenous foodstuffs in place of 40. Women in the last month of pregnancy received a ration containing between 1,700 and 1,900 calories. For all ages certain vitamins were insufficient.

Fourneau pointed out chemical deficiencies of this regimen. It was characterized particularly by poverty in calcium, phosphorus and vitamin D. These three elements constitute an inseparable ensemble. Their presence and proper relationship are indispensable not only for life but also for growth.

It has been frequently remarked that country dwellers have suffered less than city dwellers. That is correct as far as it concerns those who could make use of the provisions existing in their community. The black market was of help to those who could make use of it. A certain number of workers in heavy industries received supplementary rations. However, these allocations also were insufficient. One should not omit the mention of elderly persons, the poor of the cities and public charges.

DISEASE AND DEATH INCREASE

The situation in the prisons, in the prison camps, in the concentration camps and among the deported who returned from Germany was terrible. In one colony of liberated refugees containing about 800 persons Sivadon observed 40 cases of generalized edema resembling beriberi associated with paretic symptoms. In the prisons, which were never so crowded as they are now, because of the Gestapo, the resistance of the inmates was reduced to the point that they died not so much from hunger as from infectious diseases. The mortality was three times the normal rate. Naturally these privations were multiplied during the cold season. Intellectual workers also were victims of insufficient nourishment, as pointed out by Binet and Georges Duhamel.

This state of chronic subnutrition was bound to reflect on the general state of health of the French, their morbidity and their mortality. The mortality in 1939 amounted to 15.5; it reached 18.6 in 1940. The mortality for the period of 1939 to 1943 for ages up to 1 year progressed from 62 to 75, an increase of 19 per cent. It is said that this rate was surpassed in 1944. The consequences of the war and subnutrition are catastrophic for children. The mortality rates, however, should be considered with regard to the particular territory. When one considers, for example, the eight departments of the Mediterranean zone, which contain rural and urban populations totaling 3,410,000 inhabitants, it will be found that the mortality rate in 1938 amounted to 145 for 10,000 and a mortality rate for tuberculosis of 109 for 100,000. These figures increased for 1943 from 149 to 183 (26 per cent), and 36.8 per cent for the mortality from tuberculosis. The variations for mortality rates from contagious diseases are not significant and the figures do not include war prisoners or those dying in captivity. A more thorough investigation into the subject is necessary, because the figures thus far obtained under difficult conditions are not entirely reliable.

CHILDREN AND AGED SUFFER

For morbidity the consequences are varied. The lack of vitamins A and D have grave consequences: 54 per cent of the nurslings and infants below the age of 2 in Paris present signs of rickets. Mortality from gastroenteritis increased by 50 per cent.

Hunger edema is rather common among the aged. Loss of weight has been universally observed. It amounted for adults to as much as 25 Kg., or an average of 15 to 20 per cent. In infants it caused arrest of increase in weight. Aubertin observed that in children of Parisian schools the number of the emaciated and those whose weight did not increase amounted in 1941 and 1942 to 20 per cent. Emaciation was accompanied by fatigue. There were observed diseases of bone due to hunger; hernias and visceroptosis frequently developed; the red blood cells were often reduced to 3 or 4 million; a glycemia of 0.80, azotemia down to 0.30, indolent skin infections and disturbances of sulfur and calcium metabolism leading to spontaneous fractures were common. Fiessinger and his collaborators call attention to the frequent occurrence of miliary tuberculosis. The mortality from tuberculosis has reached alarming figures. Besides the miliary type, there occur cardiac complications and pleurisy. Pneumothorax therapy has proved to be ineffective.

Marriages

ALBERT S. WINER, Washington, D. C., to Miss Monalee Ellis of Fort Worth, Texas, November 5.

JOHN SIMPSON GORDON JR., Milwaukee, to Miss Lilfred Wright of Nashville, Tenn., February 16.

HARRIE BURTON LOCHHEAD, Philadelphia, to Miss Helen Stevenson of Oak Park, Ill., January 2.

JOSEPH HENRY MORRIS, Maysville, Ga., to Miss Rose Marie Cameron of New Orleans in December.

DAVID HUGH VARN JR. to Miss Thelma Ruth McEntee, both of Birmingham, Ala., January 27.

LAWRENCE WESTCOTT ROESSING to Miss Mabel Emily Wilson, both of Pittsburgh, February 14.

JOSEPH S. BEREZ, Redondo Beach, Calif., to Miss Ray Leslie Mann of Los Angeles, January 19.

BERNARD M. ZUSSMAN, New York, to Miss Jane Erdman of Memphis, Tenn., February 10.

GEORGE PETER HUMMEL to Miss Joan Louise Evans, both of Columbus, Ohio, February 17.

WOOD LYDA, Washington, D. C., to Mrs. Nancy Mullen Steere of Seattle, January 20.

HARRY CRAWFORD KING to Miss Lois Amy Campbell, both of Atlanta, Ga., January 6.

LEO WICKERT JR. to Miss Marie Elizabeth Slevin, both of Detroit, February 10.

W. E. FULMER, Columbia, S. C., to Miss Oney Fowler of Laurens recently.

Deaths

Terigi Richard Paganelli ✦ New York; College of Physicians and Surgeons, Baltimore, 1903; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; a founder of the New Jersey Academy of Medicine; member of the New York Academy of Medicine; at one time on the faculty of the New York Ophthalmic Hospital; consultant eye surgeon at St. Clare's and Downtown hospitals and the Northern Dispensary; honorary assistant surgeon, New York Eye and Ear Infirmary; consultant eye surgeon at the Columbus Hospital in Newark, N. J.; on the staff of the North Hudson Hospital, Weehawken, N. J.; at one time eye surgeon for the Delaware, Lackawanna and Western Railroad; served as eye examiner for the New York State Civil Service Commission in Albany and consultant eye surgeon for the New Jersey Department of Labor; during World War I president of the Italian Red Cross, member of the medical advisory board number 46 and member of draft board number 2 in Hoboken, N. J.; formerly eye surgeon for the board of education in Hoboken; composed the "University of Maryland March" and many light ballads; died in Orange, N. J., February 18, aged 63, of coronary thrombosis.

James Sprigg Wilson ✦ Colonel, U. S. Army, retired, Columbus, Ohio; University of Virginia Department of Medicine, Charlottesville, 1892; Army Medical School, 1896; entered the medical corps of the U. S. Army in 1896; rose through the various grades to the grade of colonel on May 15, 1917; retired Dec. 31, 1922 for disability in line of duty; veteran of the Spanish-American War and World War I; from 1910 to 1914 professor of tropical diseases at the University of Vermont College of Medicine, Burlington; in 1918 and 1919 chief surgeon for the American Expeditionary Forces in Siberia and also chief surgeon of the Inter-Allied Sanitary Commission; at one time surgeon for the Fifth Corps Area, with headquarters at Fort Hayes; in 1922 awarded the Distinguished Service Medal for outstanding work in the medical department of the Army; in 1921 received the master of science degree in public health at the Ohio State University, where in 1923 he became assistant professor of public health, serving in that capacity until 1933, and during 1932 and 1933 as director of the student health service; died in the Station Hospital, Fort Hayes, January 15, aged 73, of arterial hypertension.

Ralph Emerson Myers ✦ Oklahoma City; Cornell University Medical College, New York, 1918; specialist certified by the American Board of Radiology, Inc.; at one time professor of pharmacology at the University of Maryland, Baltimore, and professor of pharmacology and physiologic chemistry at the George Washington University School of Medicine, Washington, D. C.; later director of laboratories, St. Anthony's Hospital; served in the medical corps of the U. S. Army during World War I; at one time chairman of the section on radiology of the Southern Medical Association; fellow of the American College of Radiology; member of the American Radium Society, Radiological Society of North America and American Society of Clinical Pathologists; died at the Polyclinic Hospital March 14, aged 57, of meningitis caused by the type III pneumococcus.

Edith Belle Lowry ✦ St. Charles, Ill.; Bennett Medical College, Chicago, 1907; for six years a public school teacher in Minnesota and Utah; served as acting chief of the bureau of hospitals for the Chicago Health Department during World War I; from 1920 to 1923 director of field investigations in child hygiene in many Southern states under the U. S. Public Health Service division of child hygiene; in 1924 appointed chief of the division of child hygiene of the state department of public health; member of the American Public Health Association, Mississippi Valley Medical Society and American School Health Association; author of numerous books on hygiene; on the staff of the Delnor Hospital, where she died March 8, aged 66, of peritonitis.

Frank Farnum Abbott ✦ Ontario, Calif.; Jefferson Medical College of Philadelphia, 1907; served as associate professor of medicine at the College of Medical Evangelists, Loma Linda and Los Angeles; past president of the San Bernardino County Medical Society; in 1938 president of the Southern California Society for the Control of Syphilis and Gonorrhea; medical superintendent of the Paradise Valley Sanitarium and Hospital, National City, from 1910 to 1913; for many years chief of the syphilis clinic at the San Bernardino County Hospital, San Bernardino; member of the staffs of San Antonio Community Hospital, Upland, and the Pomona Valley Hospital, Pomona; died March 9, aged 61, of coronary thrombosis.

Walter Fulton Whittimore Hay, Portland, Maine; Harvard Medical School, Boston, 1924; diplomate of the National Board of Medical Examiners; member of the American Medical Association, New England Obstetrical and Gynecological Society and the New England Surgical Society; fellow of the American College of Surgeons; interned at the Boston City Hospital, where he was on the surgical staff; interned at the Boston Lying-In Hospital; served overseas with the Red Cross Ambulance Service during World War I; on the staffs of the Maine General and Children's hospitals; visiting surgeon at the Mercy Hospital and the Maine Eye and Ear Infirmary; died December 27, aged 47, of coronary occlusion.

Albert Pope Fitzsimmons, Tecumseh, Neb.; Omaha Medical College, 1895; member of the American Medical Association; past president of the Johnson County Medical Society; veteran of the Spanish-American War; later acting assistant surgeon in the U. S. Army; served for two years as surgeon general of the Nebraska National Guard and for five years in the medical reserve corps of the U. S. Army; at one time associated with the government of the Philippine Islands; a member of the board of directors of the Johnson County Bank and of the board of the Tecumseh Building and Loan Association; died February 22, aged 75, of cerebral hemorrhage, hypertension and arteriosclerosis.

Carl Foster Snapp ✦ Grand Rapids, Mich.; Rush Medical College, Chicago, 1915; interned at the Presbyterian Hospital, Chicago; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the Kent County Medical Society, Southwest Michigan Triological Society and the Grand Rapids Eye, Ear, Nose and Throat Society; specialist certified by the American Board of Otolaryngology; served in France during World War I; for many years on the staffs of St. Mary's Hospital and the Blodgett Memorial Hospital, where he died January 20, aged 57, of cardiovascular renal syndrome with hypertension and uremia.

Charles Davison Knowlton ✦ Rockport, Mass.; College of Physicians and Surgeons, Boston, 1889; Tufts College Medical School, Boston, 1894; University of Pennsylvania Department of Medicine, Philadelphia, 1895; at one time assistant professor of theory and practice of medicine at Tufts College Medical School and instructor in laryngology at Harvard Medical School, Boston; an Affiliate Fellow of the American Medical Association; specialist certified by the American Board of Otolaryngology; served on the staffs of the Massachusetts Eye and Ear Infirmary and the Massachusetts General Hospital in Boston; died January 5, aged 77, of cerebral hemorrhage.

Edward Milton Foote, New York; Harvard Medical School, Boston, 1890; formerly instructor in surgery at the Columbia University College of Physicians and Surgeons and clinical professor of surgery at the New York Polyclinic Medical School and Hospital; commander, medical corps, U. S. Naval Reserve, during World War I; at one time visiting surgeon to the New York City Hospital, New York Skin and Cancer Hospital and St. Joseph's Hospital; served as chief of surgery at the Vanderbilt Clinic; joint author of "Principles and Practice of Minor Surgery"; died in the Roosevelt Hospital February 14, aged 79, of spontaneous pneumothorax.

Edward Lovelle Stewart ✦ Kansas City, Mo.; Kansas City Medical College, 1903; for many years professor of bacteriology and histology at the Kansas City Western Dental College, which in 1941 dedicated its current year book, the *Bushwacker*, to him; at one time professor of bacteriology at the University Medical College of Kansas City; served during World War I; colonel, medical reserve corps, U. S. Army, not on active duty; founder and first editor of the *Bulletin of the Jackson County Medical Society*; on the staffs of the Willows Maternity Sanitarium and the Fairmount Maternity Hospital; died January 24, aged 68, of bronchial carcinoma.

Joseph MacDonald Bobb, Cheektowaga, N. Y.; Meharry Medical College, Nashville, Tenn., 1934; interned at the Flint Goodridge Hospital of Dillard University, New Orleans; member of the American Medical Association; state physician for syphilis control at the William Street Clinic sponsored by the Meyer Memorial Hospital and a physician in the state compensation department; served as medical examiner for the Selective Service Board number 596; on the courtesy staffs of the Mercy Hospital and the General Hospital in Buffalo; died in the Freedmen's Hospital, Washington, D. C., January 30, aged 41, of intestinal obstruction and gangrene.

Bertnard Smith ✦ Los Angeles; Rush Medical College, Chicago, 1903; clinical professor of medicine at the University of Southern California School of Medicine; member of the American Society for Clinical Investigation, the American

Heart Association and the Pacific Interurban Clinical Club; fellow of the American College of Physicians; served in the medical corps of the U. S. Army during World War I; director of the Los Angeles Metabolic Clinic; on the staffs of the Children's Hospital, Cedars of Lebanon Hospital and the Hospital of the Good Samaritan; died January 23, aged 66.

Craig Wilson Munter ✠ Fort Worth, Texas; University of Nebraska College of Medicine, Omaha, 1924; member of the American Urological Association; served as vice president of the State Medical Association of Texas; vice president and formerly secretary of the Tarrant County Medical Society; editor-manager, *Bulletin of the Tarrant County Medical Society;* consulting urologist, City and County Hospital; member of the staffs of the All Saints Episcopal Hospital and the Harris Memorial Methodist Hospital, where he died January 14, aged 44, of coronary occlusion.

Robert Oliver Tucker, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1885; member of the American Medical Association; past president of the Nashville Academy of Medicine; formerly professor of obstetrics at his alma mater and dean of the faculty and professor of obstetrics and clinical midwifery at the Medical Department of the University of Nashville and the University of Tennessee; served on the staffs of the Nashville General and St. Thomas hospitals; one of the founders of the Protestant Hospital; died January 13, aged 81, of angina pectoris.

Frank Edward Duehring ✠ Washington, D. C.; Georgetown University School of Medicine, Washington, 1912; associate professor of anesthesia at his alma mater; member of the American Society of Anesthetists, Inc.; past president of the Georgetown Clinical Society; fellow of the International Anesthesia Research Society; served as a contract surgeon at Fort Myer, Va., during World War I; chief anesthetist at the Georgetown, Episcopal Eye, Ear and Throat and Providence hospitals; died February 2, aged 55, of coronary occlusion.

Charles Eli Adams, San Jose, Calif.; Dartmouth Medical School, Hanover, N. H., 1894; died January 26, aged 81, of coronary thrombosis.

Horace Russel Frank Allen, Indianapolis; College of Physicians and Surgeons, New York, 1895; member of the American Medical Association; for many years chief surgeon of the Indianapolis Motor Speedway; died February 12, aged 76, of coronary occlusion.

David Herman Anderson, Carmel, Calif.; University of Pennsylvania School of Medicine, Philadelphia, 1925; interned at the Rochester General Hospital, Rochester, N. Y.; served during World War I; with the Rockefeller Foundation for many years; died February 9, aged 49, of cerebral hemorrhage.

Robert Louis Banister, Ralston, N. J.; Columbia University College of Physicians and Surgeons, New York, 1904; died in the Morristown Hospital, Morristown, February 2, aged 68, of heart disease.

John Frederick Bausch, Ross, Ohio; Miami Medical College, Cincinnati, 1907; member of the American Medical Association; on the staffs of the Fort Hamilton Hospital and the Mercy Hospital, Hamilton, where he died February 18, aged 62, of heart disease.

William Franklin Beck, Altoona, Pa.; Jefferson Medical College of Philadelphia, 1891; first police surgeon of Altoona; one of the founders, member of the staff and for many years member of the board of trustees of the Mercy Hospital, where he died February 8, aged 79, of injuries received when struck by an automobile.

Robert James Beels, Shaker Heights, Ohio; Bennett Medical College, Chicago, 1910; member of the American Medical Association and the Cleveland Academy of Medicine; member of the staff of the Glenville Hospital, Cleveland; served during World War I; died February 2, aged 66, of rheumatic and arteriosclerotic heart disease.

Erwin Felix Benner, Salfordville, Pa.; Medico-Chirurgical College of Philadelphia, 1899; died in the Grand View Hospital, Sellersville, January 29, aged 68, of mesenteric thrombosis.

Lon C. Bice, Edinburg, Ind.; Bellevue Hospital Medical College, New York, 1897; member of the American Medical Association; served during World War I; died March 15, aged 74, of coronary thrombosis.

Windsor Aldrich Brown, Seattle; University of Vermont College of Medicine, Burlington, 1889; member of the American Medical Association; at one time city physician and member of the school board in Worcester, Mass.; died February 3, aged 76, of heart disease.

Thomas Parker Bullard, Palmetto, Ga.; Atlanta Medical College, 1897; member of the American Medical Association; died in a hospital at Newnan January 19, aged 73, of coronary heart disease.

Charles Emery Burleson, La Porte, Ind.; Northwestern University Medical School, Chicago, 1904; member of the American Medical Association; formerly county health officer; county jail and county farm physician; on the staff of the Fairview Hospital; died February 10, aged 72, of coronary occlusion.

Sydney Howard Carney Jr., New Rochelle, N. Y.; Dartmouth Medical School, Hanover, N. H., 1889; served during World War I; died January 13, aged 81, of myocardial failure.

James Bell Carothers, Atlanta, Ga.; Atlanta Medical College, 1915; member of the American Medical Association; on the staff of the Crawford W. Long Memorial Hospital, where he died January 17, aged 55, of coronary occlusion.

Francesco Ciuccarelli, Trenton, N. J.; Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia, Italy, 1916; served with the Italian army during World War I; died in St. Michael's Hospital, Newark, February 7, aged 55, of hypertensive encephalopathy and chronic nephritis.

Roy Ellis Cruzen, Centralia, Ill.; University of Minnesota College of Medicine, Minneapolis, 1915; died December 28, aged 55.

Thomas Maltby Cunningham ✠ La Mesa, Calif.; College of Physicians and Surgeons, New York, 1895; at one time on the staff of St. Luke's Hospital in Marquette, Mich.; served on the staffs of the Mercy Hospital in San Diego and the Community Hospital; died February 6, aged 76, of cerebral hemorrhage.

Louis E. Daugherty ✠ St. Paul; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; clinical assistant professor of general surgery at his alma mater; fellow of the American College of Surgeons; chief surgeon for the Omaha Railway for many years; on the staffs of the Miller Hospital, St. Joseph's Hospital and St. Luke's Hospital, where he died January 10, aged 64, of cardiorenal disease.

Henry Louis Dietz ✠ Oakland, Calif.; California Medical College, San Francisco, 1896; died December 12, aged 71, of cardiovascular renal disease.

William L. England, Middletown, Ohio; Columbus Medical College, 1881; died January 6, aged 91, of myocardial failure.

Joseph Creighton Feindel, Athol, Mass.; College of Physicians and Surgeons, Baltimore, 1897; Harvard Medical School, Boston, 1899; died in Northampton December 20, aged 79, of coronary heart disease.

John J. Flanagan, New York; L.R.C.P. and L.R.C.S., Edinburgh, and L.R.F.P.& S., Glasgow, 1900; since 1924 head of the medical department of the New York Postoffice; at one time associated with the Bronx County Board of Health; died January 29, aged 67, of cerebral hemorrhage.

Robert Lee Gallaher ✠ Caryville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1900; past president of the Campbell County Medical Society; served during World War I; for many years surgeon for the Southern Railway; president of the First National Bank of Lake City and First State Bank of Caryville; died February 8, aged 66, of cerebral hemorrhage.

Benjamin Roscoe Gary, Newport News, Va.; University of Maryland School of Medicine, Baltimore, 1891; member of the American Medical Association; served as city coroner for many years; in 1938, on the forty-seventh anniversary of his practice in the community, was presented with a silver service from his patients; instrumental in founding the Riverside Hospital, where he served in various capacities and where he died February 13, aged 76, of chronic nephritis.

Erasmus Manford Gebhart, Los Angeles; Miami Medical College, Cincinnati, 1878; died January 19, aged 89, of cerebral hemorrhage.

Frank Grauer ✠ New York; Bellevue Hospital Medical College, New York, 1884; fellow of the American College of Physicians; at one time instructor in the Carnegie Laboratories at his alma mater; at various periods pathologist and laboratory director at the Harlem Hospital, New York City Hospital, Park Hospital and the Lutheran Hospital; died in the Presbyterian Hospital February 16, aged 80, of coronary occlusion.

John Perry Griffith ✠ Pittsburgh; Medico-Chirurgical College of Philadelphia, 1906; specialist certified by the American Board of Surgery; professor of surgery at the University of Pittsburgh School of Medicine; fellow of the American College of Surgeons; president of the staff and chief surgeon, Mercy

Hospital; chairman of the medical section of the Allegheny County Civilian Defense; died February 18, aged 61, of carcinoma of the prostate.

Eugene Joseph Hanratta, Watervliet, N. Y.; Albany Medical College, Albany, 1897; member of the American Medical Association; formerly mayor and postmaster of Watervliet; died February 5.

Randolph Samuel Harter, Schoolcraft, Mich.; Rush Medical College, Chicago, 1903; served on the courtesy staff of the Borgess Hospital and on the staff of the Bronson Methodist Hospital, Kalamazoo, where he died February 10, aged 66, of chronic valvular heart disease and chronic nephritis.

Frank Alden Haslam, Boston; Harvard Medical School, Boston, 1885; member of the American Medical Association; died December 31, aged 82, of arteriosclerotic heart disease.

William McGregor Haynes, Sherman, N. Y.; University of Buffalo School of Medicine, 1888; died in the Jamestown General Hospital, Jamestown, January 21, aged 80, of cerebral hemorrhage.

Peter Andrew Helgesen, Lake Mills, Iowa; College of Physicians and Surgeons, Keokuk, 1891; member of the American Medical Association; died in Phoenix, Ariz., January 19, aged 76, of coronary occlusion, bronchial asthma and burns of the left hand.

Sylvester Bernard Helwig, St. Louis; St. Louis University School of Medicine, 1923; died in Webster Groves, Mo., February 10, aged 48, of chronic hypertensive nephritis.

Hugh William Henry ✠ New Smyrna Beach, Fla.; University of Maryland School of Medicine, Baltimore, 1891; served as councilman in Ocala and as a director of the Marion County Chamber of Commerce; a member of the Rotary Club; died January 15, aged 77, of grip and chronic bronchitis.

Herbert Inglis Hewish, Wilkes-Barre, Pa.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1898; died in the Mercy Hospital December 25, aged 70, of diabetes mellitus and arteriosclerosis.

Henry Philip Hirsch, New York; University of the City of New York Medical Department, 1891; member of the American Medical Association; formerly medical supervisor of the department of child hygiene of the board of health; for many years in charge of the medical department of the New York Postoffice; medical examiner for the Veterans Administration at the Veterans Administration Facility; died February 19, aged 74, of coronary thrombosis.

David Ivison Hoage, New York; Long Island College Hospital, Brooklyn, 1903; died January 23, aged 67, of heart block and acute dilatation of the heart.

William Walter Hobson, Pittsburgh; College of Physicians and Surgeons, Baltimore, 1910; medical director of the Reliance Life Insurance Company; died January 4, aged 60, of coronary occlusion.

Herbert J. Hopkins, Pittsburgh; McGill University Faculty of Medicine, Montreal, Que., Canada, 1888; member of the American Medical Association; died December 14, aged 77, of coronary occlusion.

Waldo Willard Hull, South Williamsport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1889; veteran of the Spanish-American War; died December 15, aged 79, of carcinoma of the face with metastasis to the brain.

Samuel Adams Jackson, Muskegon, Mich.; Detroit College of Medicine and Surgery, 1916; member of the American Medical Association; past president of the Muskegon County Medical Society; for many years a member of the board of health; fellow of the American College of Surgeons; served as acting assistant in the U. S. Public Health Service; on the staffs of the Hackley and Mercy hospitals; died January 2, aged 54, of coronary disease.

John Knox Jamieson, Paw Paw, Mich.; Bennett Medical College, Chicago, 1900; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; on the staff of the Lake View Municipal Hospital; died January 5, aged 71, of heart disease.

Hugh David Jamison, Summit, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; at one time on the staff of the Manhattan Eye, Ear, Nose and Throat Hospital, New York; died February 12, aged 71, of heart disease.

James Colton Johnson, Cedar Rapids, Iowa; Western University Faculty of Medicine, London, Ont., Canada, 1892; died December 25, aged 76, of cardiorenal disease and chronic hepatitis.

Harry Julius Kalet, Pittsburgh; University of Pittsburgh School of Medicine, 1914; member of the American Medical Association; died in the Mercy Hospital February 18, aged 52, of rheumatic and hypertensive heart disease.

Meger Zackary Kara ✠ New York; University of Istanbul Medical Faculty, Turkey, 1914; attending ophthalmologist on the staff of the New York Eye and Ear Infirmary and chief of the department of ophthalmology at the Stuyvesant Polyclinic; died at the Jersey City Medical Center, Jersey City, February 10, aged 56, of malignant nephrosclerosis.

James C. Kelton, Lascassas, Tenn.; University of Tennessee Medical Department, Nashville, 1901; member of the American Medical Association; formerly vice president and president of the Middle Tennessee Medical Association; died January 9, aged 74, of cerebral thrombosis.

William Pitt Kennedy, Dickson, Pa.; Starling Medical College, Columbus, 1882; died December 17, aged 87, of cardiovascular disease.

William Francis Latzko, New York; Medizinische Fakultät der Universität Wien, Vienna, Austria, 1886; at one time professor at the University of Vienna and university in Buenos Aires; consultant at the Beth Israel Hospital, where he died February 11, aged 81, of cirrhosis and carcinoma of the liver.

Joseph Charles Lill ✠ Fort Wayne, Ind.; St. Louis University School of Medicine, 1918; served as a member of the city board of health and as a deputy county coroner; on the staff of St. Joseph Hospital; died in Fort Lauderdale, Fla., January 4, aged 51, of pancreatic carcinoma.

John Lewis Mahoney, St. Petersburg, Fla.; Boston University School of Medicine, 1898; member of the American Medical Association; died January 2, aged 72, of carcinoma of the sigmoid with metastasis.

John T. Manierre ✠ Chicago; Northwestern University Medical School, Chicago, 1894; died January 12, aged 75, of carcinoma of the stomach.

Guy Carlton Matthewson, Flint, Mich.; Detroit College of Medicine and Surgery, 1916; member of the American Medical Association; died in the Hurley Hospital January 20, aged 62, of carcinoma of the face.

Robert O. McAlexander ✠ Indianapolis; Medical College of Indiana, Indianapolis, 1896; served on the staff of the City Hospital; died in the Methodist Hospital January 12, aged 77, of carcinoma of the stomach.

Benjamin J. Nauman, Peru, Ill.; Rush Medical College, Chicago, 1899; died in Wichita, Kan., January 5, aged 72, of senility.

Gail Simpson Newsom, Philomath, Ore.; University of Oregon Medical School, Portland, 1904; formerly health officer of Klamath County; on the staffs of the Ball Clinic and the Corvallis General Hospital, Corvallis; died in Corvallis December 22, aged 63, of cerebral hemorrhage.

Alvin Frank Renneker ✠ Cincinnati; Ohio-Miami Medical College of the University of Cincinnati, 1911; on the staff of the Good Samaritan Hospital, where he died January 5, aged 57, of hemorrhage from gastric ulcer.

David J. Sibener ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1926; interned at the Mary Immaculate Hospital and the Queensboro Hospital in Jamaica, N. Y.; appointed diagnostician for the health department of New York City in 1929; clinical assistant of ophthalmology at Kings County Hospital and assistant in ophthalmology at the Israel Zion Hospital; died January 6, aged 42, of coronary thrombosis.

George H. Steuart, Ottoman, Va.; University of Maryland School of Medicine, Baltimore, 1899; member of the American Medical Association; served as assistant superintendent and superintendent at the University Hospital and as assistant surgeon to the U. S. Marine Hospital, both in Baltimore; chairman of the Lancaster County Board of Supervisors; died in a hospital at Richmond January 6, aged 79, of angina pectoris.

Herman W. Weinberg, Youngstown, Ohio; University of Pennsylvania Department of Medicine, Philadelphia, 1900; died in the North Side unit of the Youngstown Hospital December 31, aged 69, of arteriosclerotic heart disease.

James Corthen Woodburn ✠ Greenville, Ky.; Louisville Medical College, 1903; died January 16, aged 77, of Parkinson's disease and arteriosclerosis.

John Barnaby Woodruff, Johnstown, Pa.; Jefferson Medical College of Philadelphia, 1896; member of the American Medical Association; in 1906 president of the Cambria County Medical Society; member of the consulting staff and for many years chief of medicine at the Conemaugh Valley Memorial Hospital, where he was a member of the board of managers and where he died January 27, aged 85, of acute pyelonephritis.

DIED WHILE IN MILITARY SERVICE

Robert Ward Baker, Davenport, Iowa; State University of Iowa College of Medicine, Iowa City, 1940; member of the American Medical Association; interned at the Mercy Hospital; commissioned a first lieutenant in the medical corps, Army of the United States, on Aug. 20, 1942; later promoted to captain; died in England Nov. 23, 1944, aged 28, of pneumonia.

Wallace Rideout Briggs ✠ Sacramento, Calif.; Harvard Medical School, Boston, 1919; specialist certified by the American Board of Ophthalmology; interned at the Massachusetts Eye and Ear Infirmary; served on the staff of the Sutter General Hospital; commissioned a lieutenant commander in the medical corps of the U. S. Naval Reserve on Sept. 10, 1942; died in the U. S. Naval Hospital, Long Beach, Dec. 18, 1944, aged 50, of bronchiogenic carcinoma of the lung.

Arthur Stevenson Clay Jr., Monessen, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1938; member of the American Medical Association; interned at the George F. Geisinger Memorial Hospital, Danville, and served a residency in ophthalmology at the Wills Hospital in Philadelphia; on the staff of the Gemmill Hospital; commissioned a first lieutenant in the medical corps, Army of the United States; later promoted to captain; died in Guadalcanal Dec. 11, 1944, aged 31, of acute yellow atrophy of the liver.

William Johnston Collie, Portland, Ore.; Northwestern University Medical School, Chicago, 1936; member of the American Medical Association; interned at the Multnomah Hospital and served a residency at St. Vincent's Hospital; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on May 31, 1938; began active duty as a captain in the Army of the United States on Dec. 30, 1940; later promoted to major and lieutenant colonel; died in Schirmeck, France, January 5, aged 35, as the result of injuries incurred in an accidental collision between a tank and a jeep.

George Foster Eubanks, Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1925; interned at the Wesley Memorial Hospital; formerly fellow in surgery of the Mayo Foundation in Rochester, Minn.; at one time chief resident physician at the Knoxville General Hospital, Knoxville, Tenn.; attending proctologist at the Grady Municipal and the Georgia Baptist hospitals and associate surgeon at the Albert Steiner Clinic for Cancer and Allied Diseases; member of the American Medical Association, Association of Resident and Ex-Resident Physicians of the Mayo Clinic, Southern Medical Association and Southeastern Surgical Congress; fellow of the American Proctologic Society; in 1936 vice president of the Fulton County Medical Society; specialist certified by the American Board of Surgery; commissioned a major in the medical corps, Army of the United States, on Dec. 28, 1942; began active duty on Jan. 14, 1943; later promoted to lieutenant colonel; died in Marlborough, England, Sept. 25, 1944, aged 44, of coronary occlusion.

Sydney Charles Feinberg ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1919; interned at the Mount Sinai Hospital and the Montefiore Home and Hospital; commissioned a captain in the medical corps, Army of the United States, on July 10, 1942; died in the Tilton General Hospital, Fort Dix, N. J., Dec. 24, 1944, aged 50, of histoplasmosis.

Herbert Julius Kaufman ✠ Owosso, Mich.; Wayne University College of Medicine, Detroit, 1939; interned at the Eloise Hospital, Eloise; commissioned a first lieutenant in the medical corps, Army of the United States, on June 23, 1942; later promoted to captain; died in the Hammond General Hospital, Modesto, Calif., Nov. 20, 1944, aged 32, of meningitis.

James Floyd Klock, Billings, Mont.; University of Michigan Medical School, Ann Arbor, 1931; interned at the Harborview Hospital in Seattle; served as senior physician, U. S. Indian Service; commissioned a first lieutenant in the medical reserve corps of the U. S. Army on Feb. 13, 1933; began active duty as a captain in the medical corps, Army of the United States, on June 12, 1942; later promoted to major; died in Newbury, England, Dec. 12, 1944, aged 40, in a glider crash accident.

John Ross Marshall ✠ West Somerville, Mass.; Harvard Medical School, Boston, 1918; diplomate of the National Board of Medical Examiners; member of the New England Obstetrical and Gynecological Society; fellow of the American College of Surgeons; interned at the Boston City Hospital; served as chief surgeon at the Somerville Hospital, and on the staffs of the Cambridge Hospital, Cambridge, Lawrence Memorial Hospital, Medford, and the Symmes Arlington Hospital, Arlington; college physician for Tufts College for seventeen years; served during World War I, entering the U. S. Naval Reserve in 1918, subsequently serving a temporary assignment in the U. S. Navy as a lieutenant; later became a lieutenant and lieutenant commander in the medical corps of the U. S. Naval Reserve; reentered active service in May 1941, serving since Jan. 23, 1943 as medical inspector with the rank of commander; served at the U. S. Naval Hospital, Chelsea, and at U. S. Naval Hospital, Shoemaker, Calif., where he died Oct. 14, 1944, aged 56, of Staphylococcus aureus septicemia.

Fabian Lee Pratt ✠ Colonel, M. C., U. S. Army, San Francisco; Vanderbilt University School of Medicine, Nashville, 1911; School for Flight Surgeons in 1921, Air Service Balloon and Airship School, 1923, and Air Corps Primary Flying School, 1927; interned at the Bellevue Hospital in New York; entered World War I early in 1914 with the British, serving in France and Italy until 1917, when America entered into the war, and was transferred to the United States Army; commissioned a captain in the medical corps of the regular Army in 1917; advanced through the subsequent ranks to colonel; served as a flight surgeon at various stations in the continental United States, such as Mitchel Field, N. Y., Scott Field, Ill., Fort Riley, Kan., and Bolling Field, Washington, D. C.; also served a tour of duty in Hawaii; his early association with aviation gave him insight into the problems of medicine in relation to the flier; after study of the mechanics of aviation he became the only medical officer in the Army to hold pilot ratings in air craft both lighter than air and heavier than air; the Research Laboratories of the School of Aviation Medicine are a tribute to his efforts, as he was among the first to think in terms of research as applied to aviation medicine; served as commandant of the School of Aviation Medicine, 1939-1941; as a pilot he had over three thousand flying hours to his credit and was active in aviation almost to the day of his death; authorized to wear the Purple Heart, the Victory Medal, the King George Medal, the Belgian and Italian war crosses and many other decorations; since February 1943 surgeon of the Fourth Air Force; died December 18, aged 55, of heart disease.

Henry Matthew Usiak, Buffalo; University of Buffalo School of Medicine, 1941; diplomate of the National Board of Medical Examiners; interned at the Edward J. Meyer Memorial Hospital; commissioned a first lieutenant in the medical corps of the Army of the United States on June 11, 1941; later promoted to captain; died in Italy Nov. 30, 1944, aged 27, of infectious hepatitis.

Jesse H. West ✠ San Francisco; University of Oregon Medical School, Portland, 1926; interned at St. Luke's Hospital, where he was later chief resident; commissioned a captain in the medical corps, Army of the United States; died in the Lawson General Hospital, Atlanta, Ga., February 4, aged 46, of brain tumor.

Frederick Ray Woodward, Los Angeles; Medical College of Virginia, Richmond, 1942; served an internship and residency at the Los Angeles County Hospital; commissioned a first lieutenant in the medical corps, Army of the United States, June 2, 1942; died in Abilene, Texas, Nov. 22, 1944, aged 30, in an aircraft accident.

Bureau of Investigation

NEW NAMES FOR OLD SWINDLES

Mail-Order Defrauders Are Also Repeaters

Fraud orders issued by the United States Post Office are really effective—so far as the trade styles and names used at the time of the order are concerned. Circumvention therefore requires the use of new trade styles and names—but this fortunately results in the issuance of supplemental orders by the Post Office Department as indicated in the following paragraphs:

A. L. Dean, Robert Probasco, "Arthritis" and C. E. Charts.—The Probasco in question was known as the general manager of a Los Angeles concern operating under the names "American Mutual Health Association" and "ABC Preparations Company," selling "A B C Preparations" through the mails with the representation that these would "cure" all forms of rheumatism, sciatica and arthritis when used according to directions in conjunction with "diet charts" and "instruction sheets" furnished by the promoters. As shown in this department of The Journal July 8, 1944, page 737, the Post Office Department debarred the scheme from the mails as a fraud. It was also shown that according to a government chemist, one part of the treatment was chiefly water, with less than 1 per cent each of hydrochloric and nitric acids; another contained 36 per cent of alcohol and small amounts of Jamaica dogwood and cimicifuga, and the third, a powder, was a mixture of phenolphthalein, senna, sulfur and cream of tartar. The Post Office Department, however, later learned that Probasco had continued the business under his own name and that of an A. L. Dean, and on May 20, 1944, the Post Office issued a fraud order against these two names. Even this did not put an end to the fraud, for it was next discovered that Probasco was still doing business at the old address, 326 West Third Street, Los Angeles, but under a new trade style, "Arthritis." Against this name, accordingly, the Post Office Department issued a fraud order on Dec. 5, 1944. Nor was this all. Probasco, as might have been expected, adopted a new trade style, "C. E. Charts," and on stickers attached to advertising matter that he sent out to prospects and old customers, he urged them to use only that title in addressing him. The Post Office Department, however, soon caught up with this trick, and on Jan. 30, 1945, issued an additional fraud order covering the name C. E. Charts. A further one was issued on Feb. 24, 1945 against "Diet Charts," the new name that Probasco had adopted. Again he changed his trade style, this time to "Correct Diet," and on March 21, 1945, a fraud order was issued against this name. Very likely, however, the end is not yet, and one can only speculate on how many more fraud orders the government will have to issue against Probasco before he decides to give up his swindles.

E. J. McCann.—This department of The Journal, July 9, 1938, p. 188, gave details of the case in which E. J. McCann of Elmira, N. Y., was debarred from the use of the mails under his name and that of "Tonsol." The bone of contention was an alleged cure for diphtheria and tonsil infections, which treatment McCann sold through the mails and which the Post Office Department declared fraudulent. Government chemists reported that their analysis of Tonsol showed it to be essentially a 15 per cent solution of mild silver protein (argyrol type). At the hearing of the case it had also been shown that McCann was without medical education or training, and that no one with such qualifications was connected with his business. The article stressed the danger, not only to the individual but to the community, of attempting to treat diphtheria with a spray sold on the mail-order plan. Since the order debarring McCann's business from the mails covered even his personal mail, on March 14, 1940, he filed with the Post Office Department an affidavit to the effect that his Tonsol activities had been discontinued and would not be resumed, either under the names formerly used or any others. Accordingly, the Post Office Department revoked the original fraud order to the extent of permitting McCann to receive personal mail in no way relating to his former business. Some time later, however, the Post Office Department, after obtaining evidence that McCann had resumed his old scheme and was selling a nostrum similar to Tonsol through the mails under the name "McCann's Remedy," ordered him to show cause why a new fraud order should not be issued against him. This he was unable to do to the satisfaction of that Department, and on Sept. 7, 1944, the order was issued against the names McCann, E. J. McCann, "McCann's Remedy," and their officers and agents. It is worth noting that another government agency, the Food and Drug Administration, had occasion to prosecute McCann, also trading as the Tonsol Company, for fraudulently representing on the label of his nostrum that it was an effective cure for diseased tonsils, diphtheria, adenoids, quinsy and some other things. The government's report of this case stated that on Jan. 10, 1939, McCann entered a plea of *nolo contendere*, and the district federal court in which the case was tried imposed a fine of $50 but suspended payment thereof and placed McCann on probation for three months.

Juan Avina.—From Madero, Mexico, one Juan Avina, using the names The Invisible Hospital and The Invisible Doctors, perpetrated a fraud through the United States mails in representing that for certain sums he would prescribe curative treatment for any diseases and that through his "invisible mystic power" he would "follow" the patient everywhere and protect him against all harm. The scheme was particularly directed to residents of Puerto Rico. On Oct. 4, 1940, the Post Office Department at Washington issued a fraud order against Avina's scheme, debarring it from the United States mails. Later investigation revealed that Avina was evading the fraud order in continuing his business and operating under the names Vina, Abinia, Abina and Avina and still operating from Madero. Accordingly, on Oct. 23, 1944, the Post Office Department extended the original fraud order to cover these names.

Correspondence

SPONTANEOUS PNEUMOTHORAX AND ASCENT IN AIRPLANE

To the Editor:—In The Journal, March 3, Holter and Horwitz reported an instance of spontaneous pneumothorax produced by ascent in an airplane. In considering the mechanism of this accident the authors make the following statements: "Under normal conditions the pleural cavity is merely a potential space between the parietal and pulmonary pleura in which an average pressure of about 756 mm. of mercury is maintained. Again under normal conditions the intrapulmonary pressure is kept at approximately the same level. In this case the pressure was rather abruptly dropped to about 560 mm. of mercury or by about 26 per cent, thereby creating a tendency for the lung to collapse partially. As long as the pleural cavity remained potential, this would not have been possible. But with the development of increased tendency to separate the pulmonary from the parietal pleura a weakness in the pleura was exploited and pneumothorax occurred." This reasoning contains a fundamental error which should be corrected, since the authors have expressed an opinion that extreme caution is warranted in advising patients who have had known diseases of the pleura about airplane travel.

With decrease in atmospheric pressure, the absolute pressure in the tissues of the body decreases correspondingly, so that the tissue pressure relative to atmospheric pressure remains the same (Ferris, E. B.; Molle, W.; Engel, G. L.; Webb, J. P., and Blankenhorn, M. A.: Unpublished data). Liquids show no volume change under these conditions. The only way in which liquid tissues can change in volume is through the formation of tissue bubbles as the result of a relatively rapid exposure of the body to low atmospheric pressure. This phenomenon, which is responsible for the syndrome of decompression sickness, does not occur at altitudes much below 20,000 feet and could not be a factor in this subject who reached only 8,000 feet. High altitude likewise has no effect on the volume or pressure of air or gas containing structures as long as they are in free communication with the ambient atmosphere (i. e. the lungs). Changes in pressure and volume will occur only in gas containing structures that have inadequate or no communication with the external atmosphere (i. e. middle ear, paranasal sinuses, gastrointestinal tract). As long as there is no air in the pleural space there will be no relative change in intrapulmonary pressure and hence no "tendency for the lung to collapse partially." Similarly, an emphysematous bleb would not be any more likely to rupture at altitude unless it had little or no communication with intrapulmonary air.

Hence it seems reasonable to conclude that ascent to altitude cannot act as a precipitating factor for spontaneous pneumothorax by the mechanism the authors suggest. Indeed, if such a mechanism was possible one might expect a much higher incidence of spontaneous pneumothorax during the millions of airplane ascents that have been made in the past five years. Actually, it seems doubtful that the incidence is any higher than among the nonflying population. The tendency toward pneumothorax would be increased only if there already was air in the pleural space or in the pulmonary interstitial tissue or mediastinum, a mechanism for pneumothorax pointed out by M. T. Macklin and C. C. Macklin (*Medicine* **23**:281, 1944).

It seems likely either that the occurrence of pneumothorax in this subject was coincidental to flight or that the subject already had a pneumothorax before ascent.

George L. Engel, M.D.
Eugene B. Ferris, M.D.
University of Cincinnati College of Medicine,
Cincinnati.

To the Editor:—I wish to comment on the article of Holter and Horwitz on "Spontaneous Pneumothorax Produced by Ascent in an Airplane" (THE JOURNAL, March 3, p. 519). They state that the intrapleural pressure in the potential space falls from 756 mm. of mercury to 560 mm. of mercury by ascent from the ground to an altitude of 8,000 feet, "thereby creating a tendency for the lung to collapse partially." I believe that the latter statement is untrue, for actually the only factor tending to separate the visceral and parietal pleurae is the elastic pull of the lung tissue. At any altitude and all altitudes, with the visceral and parietal pleurae in apposition and the pleural space merely a potential one, atmospheric pressure exerts an equal push on the inside of the visceral pleura and the outside of the parietal pleura. At any elevation it is only the elastic pull of the lung tissue which tends to separate the pleurae or to tear a weak place in the pleura.

Their second possibility "is that a peripheral emphysematous bleb may have ruptured as the result of relative increase of pressure within the bleb itself." I would go further and maintain that the only physical possibility of producing pneumothorax by ascent in an airplane would be by the expansion of gas in a closed bleb with consequent rupture of the part of the visceral pleura forming the portion of the wall of the bleb which is in apposition to the potential pleural space. If the bleb were open (i. e., in communication with an open bronchus) rupture could not occur. Only in a closed bleb would decreasing atmospheric pressure cause expansion of retained gas, stretching and subsequent rupture of the bleb.

It may be interesting to postulate, from the laws of physics, that coughing or straining with a closed glottis would be of great hazard to the person with an open bleb, whereas flying in an airplane would be innocuous. However, if the bleb remained closed through plugging of its bronchus the patient could cough or strain with impunity and ascent in an airplane would be likely to produce spontaneous pneumothorax.

The fact remains that, as the authors intimate, no one suspected of having emphysematous blebs or pulmonary cavities should travel by plane.

MAXWELL BERRY, M.D., Atlanta, Ga.

To the Editor:—In a recent report of a case of spontaneous pneumothorax (THE JOURNAL, March 3), Holter and Horwitz present certain statements which deserve comment.

In considering the mechanism of the accident they propose that the precipitating factor was the drop in barometric pressure entailed in an ascent to 8,000 feet, "thereby creating a tendency for the lung to collapse partially" and, again, ". . . with the development of increased tendency to separate the pulmonary from the parietal pleura, a weakness in the pleura was exploited and pneumothorax occurred." Such an increased tendency toward pulmonary collapse on ascent to altitude would indeed be an important factor to consider, if it really existed. As a matter of fact, no such tendency exists.

Under normal conditions the pressure in the potential pleural space is less than the intrapulmonary pressure by an amount which depends on the elastic recoil of the lung. The actual absolute pressure in this space is of no significance if considered alone, the intrapleural pressure being physiologically important only in relation to the intrapulmonary pressure. On ascent to altitude the intrapulmonary pressure falls, to be sure, but, since the reduction in barometric pressure is transmitted equally and immediately to all the body tissues, the intrapleural pressure remains precisely the same in relation to the intrapulmonary pressure as it was at ground level. There is no increased tendency for pulmonary collapse.

Since, as the authors point out, it seems likely that air travel will become more prevalent after the war, it is important that physicians realize the fundamental principles involved in exposure to reduced barometric pressure. Fallacious reasoning with regard to pressure relations in the body can be largely avoided if it is remembered that the tissues of the body transmit the existing atmospheric pressure immediately and equally in all directions and that such pressures as arterial and venous blood pressures, cerebrospinal fluid pressure and intrapleural pressure are measured in relation to the pressure of the ambient atmosphere. Reference to the writings of Paul Bert in the latter portion of the last century is indicated in this respect.

WILLIAM V. WHITEHORN, M.D., Columbus, Ohio.

POSTPARTUM MASSAGE OF DEEP PELVIC MUSCLES

To the Editor:—Dr. E. H. Terrell, whom I remember with pleasant memories from internship days, in THE JOURNAL, Oct. 28, 1944 calls attention to the work of Dr. George Thiele, whose "contribution . . . is the most valuable given in our field (proctology) during the past decade." Also in the field of obstetrics it has been a most valuable contribution. I have found it to be of great benefit in the late postpartum care of the obstetric patient.

So often, after delivery, there are vague sacroiliac and sacrococcygeal pains. Palpation of the deep pelvic muscles will reveal them to be spastic and painful. The trauma incident to delivery is the most likely explanation. Massage of these muscles by rectum with the patient in the lithotomy position usually gives gratifying relief. Particularly so is this if there has been undue displacement of the coccyx.

As Thiele emphasizes, massage at first should be light and of short duration, progressively increasing the pressure and length of time of treatment as the spasticity of the muscles relaxes.

Similar pain in the nonpuerperal woman has also sometimes yielded to this therapy.

WALTER S. L. MCMANN, Captain, M. C., A. U. S.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Basic Science Acts: Validity of New Mexico Act.—Polhemus, who was licensed to practice naturopathy in Arizona, without complying with the licensing laws of New Mexico attempted to practice naturopathy in that state and was arrested for practicing without a certificate from the New Mexico Board of Examiners in the Basic Sciences. Thereafter he instituted an action for damages in the district court of the United States for the district of New Mexico against the American Medical Association, the New Mexico Medical Society and the individual members of the New Mexico Board of Examiners in the Basic Sciences, which consisted of one physician, one osteopath, one chiropractor and two "laymen learned in the basic sciences." He alleged (1) that the defendants by illegal means induced the New Mexico legislature in 1941 to enact the New Mexico basic science act for the purpose of creating a monopoly in the practice of the healing arts in the state; (2) that the basic science act was discriminatory against him in that it did not entitle him, as a naturopath, to a basic science certificate on the same basis as physicians, osteopaths and chiropractors because the act, while it provided that persons licensed to practice at the time of its enactment in 1941 could receive such a certificate without examination, it made no such provision for naturopaths, who could not have been lawfully licensed as such in New Mexico at the time of the enactment of the law; (3) that the members of the basic science board adopted discriminatory and unreasonable rules and regulations in placing the basic science act into operation; and (4) that these acts together with his

arrest, which was caused by the members of the board, deprived him of his right to practice "his profession" to his damage. From an adverse judgment, Polhemus appealed to the circuit court of appeals, tenth circuit.

The trial court sustained a motion by the American Medical Association to quash service of summons as to it on the grounds that the American Medical Association is an Illinois corporation, that it is not engaged in business in New Mexico and that it has no officer in the state on whom service of process can be had. Polhemus contended that the American Medical Association was engaged in business in New Mexico through the New Mexico Medical Society and its agents and representatives. It is not necessary, said the court, to pass on this contention because in any event the summons was insufficient to bring the American Medical Association into court. The marshal's return stated that he had served a summons "on Dr. C. A. Miller for the American Medical Association, a corporation, at Clovis, New Mexico, by leaving with him personally a copy of said summons together with a copy of the complaint attached." The affidavit filed by the American Medical Association in support of its motion to quash specifically denied that Dr. Miller was an agent of the American Medical Association and the marshal's return does not show that he served him as the agent of the Association. The service therefore did not bring the American Medical Association into court.

The theory, continued the court, on which Polhemus seeks to invoke the jurisdiction of the court is not clear. The complaint alleged in general terms that the action involved violation of his rights under the constitution of the United States. Plaintiff's theory evidently was that the passage of the basic science law and its administration by the individual defendants contravened rights granted by the United States Constitution. Federal jurisdiction does not arise merely because an averment is made as to the existence of a constitutional question. A genuine and substantial federal question must be presented by the complaint. Admittedly, the police power of a state extends to the right to regulate trades and callings concerning public health. Practitioners of the healing art are properly subject to police regulation, the details of which are primarily with the legislature and not to be interfered with by the federal court so long as fundamental constitutional rights are not violated. Unless the regulations are so utterly unreasonable and extravagant in their nature and purpose that the property and personal rights of the citizens are unnecessarily and, in a manner wholly arbitrary, interfered with or destroyed without due process of law, they do not extend beyond the power of the state to pass and they form no subject for federal interference. Tested by these principles, Polhemus's complaint wholly fails to establish the existence of a federal question. There is a complete absence of any showing that the basic science act as passed, or the manner in which it is being administered, is arbitrary or capricious. The mere fact that the act does not afford plaintiff the benefit of the so-called "Grandfather Clause" (referring to the provision in the act authorizing the issuance of basic science certificates without examination to practitioners of the healing art licensed at the time the act went into effect) does not establish arbitrariness or unreasonableness. The matter of classification is for the state legislature and cannot be interfered with by a federal court in the absence of a clear showing that the adopted classification is unwarranted and unreasonable. There are no facts alleged in the complaint in this cause which would support such a finding.

There is a further attempt, continued the court, to bring the action within the terms of the Sherman antitrust act. Conceding without deciding that the practice of the healing art may constitute commerce within the meaning of the act, all of the allegations show that all the transactions relate to the practice of the healing art wholly within the state of New Mexico. Polhemus's entire practice is confined to the state of New Mexico, and the basic science law deals with the basic science act of New Mexico. Under no circumstances can such a practice be considered commerce or affecting commerce within the meaning of the Sherman antitrust act.

For the reasons stated, the judgment of the trial court dismissing the complaint was affirmed.—*Polhemus v. American Medical Association, 145 F. (2d) 357 (1944).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, March 24, page 735.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery 4.

ALASKA: Juneau, September. Sec., Dr. W. M. Whitehead, Box 561, Juneau.

ARIZONA: * Phoenix, April 3-4. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Eclectic.* Little Rock, June 7. Sec., Dr. C. H. Young, 1415 Main St., Little Rock. *Medical.* Little Rock, June 7-8. Sec., Dr. D. L. Owens, 701 Main St., Little Rock.

CALIFORNIA: *Oral.* San Francisco, May 20. *Written.* San Francisco, July 9-12. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

DELAWARE: *Examination.* Dover, July 10-12. *Reciprocity.* Dover, July 17. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

FLORIDA: * Jacksonville, June 25-26. Sec., Dr. Harold D. Van Schaick, 2736 S. W. Seventh Ave., Miami 36.

IDAHO: Boise, July 10. Dir., Bureau of Occupational Licenses, Miss Agnes Barnhart, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, April 3-5. Superintendent of Registration, Department of Registration and Education, Mr. Philip Harman, Springfield.

INDIANA: Indianapolis, Aug. 28-30. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis 4.

KANSAS: Kansas City, June 27-28. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City 10.

KENTUCKY: Louisville, June 18-20. Sec., State Board of Health, Dr. Philip E. Blackerby, 620 S. Third St., Louisville 2.

LOUISIANA: June. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans 12.

MARYLAND: *Medical.* Baltimore, June 19-22. Sec., Dr. J. T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 19-20. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MINNESOTA: * Minneapolis, April 17-19. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 2-4. Sec., Dr. O. G. Klein, First Nat'l. Bank Bldg., Helena.

NEW JERSEY: Trenton, June 19-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 9-10. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NORTH DAKOTA: Grand Forks, July 3. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* Columbus, April. *Examination.* Columbus, June. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, June 14-16. Sec., Dr. J. D. Osborn, Jr., Frederick.

OREGON: * *Reciprocity.* Portland, April 28. Sec., Dr. L. S. Besson, 608 Failing Bldg., Portland 4.

PENNSYLVANIA: April 10-13. Act. Sec., Bureau of Professional Licensing, Department of Public Instruction, Mrs. M. G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, April 5-6. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 25-27. Sec., Dr. N. B. Heyward, 1329 Blandina St., Columbia.

SOUTH DAKOTA: * Pierre, July 17-18. Sec., Medical Licensure, State Board of Health, Dr. Gilbert Cottam, State Capitol, Pierre.

TEXAS: Galveston, June 4-6. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

VERMONT: Burlington, June. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: * Richmond, June 20-23. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WASHINGTON: * Seattle, July 16-18. Sec., Department of Licenses, Miss Nell Adams, Olympia.

WISCONSIN: * Milwaukee, June 26-28. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: Little Rock, April 17. Sec., Dr. D. L. Owens, Harrison.

CONNECTICUT: June 9. Address State Board of Healing Arts, 250 Church St., New Haven 10.

DISTRICT OF COLUMBIA: Washington, April 23-24. Sec., Commission on Licensure, Dr. G. C. Rubland, 6150 E. Municipal Bldg., Washington 1.

FLORIDA: DeLand, June 1. Final date for filing application is May 17. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, April 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, May 11-12. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

MINNESOTA: Minneapolis, April 3-4. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis 14.

NEBRASKA: Omaha, May 1-2. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: Oklahoma City, April 9. Sec., Dr. J. D. Osborn, Jr., Frederick.

SOUTH DAKOTA: Yankton, June 19. Sec., Dr. G. M. Evans, Yankton.

WISCONSIN: Madison, April 7. Sec., Professor R. N. Bauer, 152 W. Wisconsin Ave., Room 834, Milwaukee 3.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

14:157-180 (Jan.) 1945

Spastic Colon. W. L. Miller.—p. 257.
Discussion of Abortion, Septic and Nonseptic. T. M. Boulware and C. D. Howe—p. 161.
*Blood Calcium and Calcium Therapy. E. H. Planck.—p. 165.

Blood Calcium and Calcium Therapy.—Planck determined the blood calcium level by the Clark-Collip modification of Tisdall's method in his own office laboratory. He suggests that the serum be allowed to stand for at least twelve hours before the test is made. His experience has been that tests run on serum standing for only four hours will frequently give a higher calcium content than specimens which have stood for at least twelve hours, thereby failing to disclose an actual deficiency. It is advisable to use only fasting blood specimens in making the blood calcium determination, and normal is considered to be 9 to 11 mg. per hundred cubic centimeters. In one year the author has detected 30 patients with low blood calcium. Most of the histories obtained were suggestive of arthritis or neuritis, although these conditions could not be found on physical examination. Some of the principal complaints were pain either just above or below joints in the bones and pain in the muscles of the legs, arms, feet and hands. Other symptoms were insomnia, dizziness, nervous irritability, emotional instability, nausea, attacks of syncope, carious and brittle teeth, ridges in the nails, fine tremor of the fingers and shortness of breath. Treatment was intravenous administration of 10 cc. of 10 per cent calcium gluconate solution on alternate days until six doses had been given. Oral therapy in the form of 10 grains (0.65 Gm.) of dicalcium phosphate with viosterol three times daily was begun and continued for at least one month. The patient was placed on a high calcium diet, and oral administration was discontinued at the end of one month, the diet being sufficient to maintain an adequate serum calcium. Borderline deficiency of calcium may be overlooked and the complaints caused by it may be attributed to malingering or to hypochondriasis or confused with symptoms of arthritis or rheumatism.

American Journal of Public Health, New York

35:1-88 (Jan.) 1945. **Partial Index**

Medical Care in National Health Program. H. R. Leavell.—p. 15.
Housing and Public Health. C.-E. A. Winslow.—p. 18.
*Making Food Handlers Health Conscious. H. A. Morgan Jr.—p. 28.

Making Food Handlers Health Conscious.—According to Morgan and his associates legislation and enforcement have failed to achieve satisfactory results in controlling food sanitation. Frequent inspection and education constitute the only effective method. With the inauguration of the Second Army maneuvers in Middle Tennessee the sanitation of food handling became a public health responsibility of primary importance because of the large number of troops served in public eating places, the increase in war workers eating out, the necessity for the adjustment of small establishments to handle large increases in patronage and the large number of novices in the business of feeding the public. A district health department was organized in the area immediately surrounding Camp Forrest. To overcome the resentment of inspection visits, a series of food handler schools was organized. Local interest in having a course was stimulated by the local sanitarian on his routine inspection visits and by the reports from centers which had participated in the course. Registration blanks are used to gain a perspective of the type of food handler group, whether local or transient, and the number and proportion of establishments represented. The registration blanks were then arranged to form a class roster to check attendance for the awarding of the certificate of attendance which was given on the basis of presence at both sessions. The food handlers' registration blanks were made a part of the permanent office files and were often valuable for later follow-up and epidemiologic investigation. The course was divided into two sessions of two hours each. The first session is summarized as the "why's of food sanitation" and the second as the "how's of food sanitation."

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

29:1-140 (Jan.) 1945

*Penicillin Treatment of Early Syphilis Resistant to Arsenic and Bismuth. R. A. Nelson and L. Duncan.—p. 1.
Optimal Carbon Dioxide Tensions for Primary Isolation of Gonococcus. W. Ferguson.—p. 19.
In Vitro Tolerance of Gonococcus for Penicillin. C. E. Lankford.—p. 56.
Use of a Solid Medium for Transportation of Specimens for Gonococcus Culture. Nell Hirschberg.—p. 64.
Infectivity of Hemophilus Ducreyi for Rabbit and Development of Skin Hypersensitivity. Rose R. Feiner and F. Mortara, with collaboration of Esther Levenkron.—p. 71.

Penicillin in Treatment of Early Syphilis.—Nelson and Duncan report the immediate results of penicillin treatment of 6 patients with early syphilis resistant to arsenic and bismuth compounds. Each of the patients had early syphilis and in all the cutaneous and genital lesions had shown either progression or failure to heal while under treatment with adequate amounts of trivalent arsenicals, usually combined with bismuth. The cutaneous lesions in all of the patients were of the psoriasiform type, and spirochetes could be demonstrated in the material from their lesions in 5 of the 6 patients. In general, treatment with penicillin was carried out in a manner similar to that used for patients with early syphilis who had not had previous arsenotherapy. Varying dosage schedules were employed. On the basis of available information, patients with arsenic-bismuth resistant syphilis should receive 2,400,000 units of penicillin intramuscularly in sixty injections of 40,000 units each given every three to four hours day and night. Cutaneous or febrile Herxheimer reactions were observed within the first twenty-four hours in 2 patients. Spirochetes disappeared from all lesions in ten to twenty-six hours after onset of treatment. The cutaneous and genital lesions usually showed prompt healing. Arsenic-bismuth resistant syphilis represents a public health hazard, because these patients are infectious. This infectiousness is quickly controlled by penicillin.

Archives of Dermatology and Syphilology, Chicago

51:1-80 (Jan.) 1945

Abnormalities of Pigmentation in Negro. M. L. Niedelman.—p. 1.
*Erythema Multiforme: Its Relationship to Herpes Simplex. N. P. Anderson.—p. 10.
Nutritional Dermatoses in Rat: XI. Vitamin A Deficiency Superimposed on Vitamin B Complex Deficiency. M. Sullivan and Virginia J. Evans.—p. 17.
Treatment of Lupus Erythematosus Disseminatus by Internal Administration of Iodine. A. B. Cannon.—p. 26.
Acrodermatitis Atrophicans Chronica. H. Montgomery and R. R. Sullivan.—p. 32.

Erythema Multiforme and Herpes Simplex.—Anderson says that for the past ten years repeated vaccination with smallpox vaccine has been utilized as a therapeutic procedure in the prevention of recurrent herpes simplex. It has been successful in about 80 per cent of the cases. Even in the 20 per cent in which failures have resulted the succeeding attacks of herpes simplex were milder for most of the patients. In the past few years Anderson has utilized such repeated vaccinations for the preventive therapy of erythema multiforme associated with herpes simplex and also in the treatment of erythema multiforme in which no such association could be determined. This procedure has been of definite value in the prevention of recur-

rences of erythema multiforme, especially that preceded by herpes simplex. He believes that this procedure should be used in cases of recurrent erythema multiforme unassociated with herpes simplex.

Archives of Ophthalmology, Chicago

33:1-96 (Jan.) 1945

Elementary Illumination for Ophthalmologist. LeG. H. Hardy and Gertrude Rand.—p. 1.
Analysis of Cases of Aniseikonia. Beulah Cushman.—p. 9.
Unusual Forms of Nystagmus, with Review of Literature. H. C. Smith and F. R. Riesenman.—p. 13.
Dibutoline Sulfate: New Mydriatic and Cycloplegic Drug. K. C. Swan and N. G. White.—p. 16.
Estimation of Uncorrected Visual Acuity in Malingerers. H. Eggers. —p. 23.
Quereau-Putnam Tropophorometer. J. V. Quereau and O. A. Putnam. —p. 28.
Hydrogen Ion Concentration of Vitreous in Living Eye. L. von Sallmann with technical assistance of Jeanette Di Grandi.—p. 32.
After-Image Perimetry: Rapid Method of Obtaining Visual Fields; Preliminary Report. W. P. Williamson.—p. 40.
Penetration of Penicillin in Rabbit Eyes with Normal Inflamed and Abraded Corneas. I. H. Leopold and W. O. LaMotte Jr.—p. 43.
Epidemic Keratoconjunctivitis. A. E. Braley.—p. 47.
Brucellosis. H. J. Harris.—p. 56.
*Sulfadiazine in Treatment of Dacryocystitis of Newborn. G. V. Simpson. —p. 62.
Optochiasmic Arachnoiditis. E. Hartmann.—p. 68.

Sulfadiazine in Dacryocystitis of Newborn.—Simpson states that the treatment of simple epiphora or epiphora complicated by dacryocystitis occurring soon after birth is based on the premise that an obstruction is present along the nasolacrimal duct. There may be either an anatomic or an accidental obstruction. A review of the causes has shown that there is a factor of infection in all cases. This factor may be primary, in which case the entire process is dependent on bacterial invasion of the mucous membrane of the nose and the nasolacrimal duct. The infection may be secondary, in which case the underlying anatomic obstructive agent favors infection by insufficient drainage of the tears. Simpson states that when a case of congenital epiphora with dacryocystitis is seen for the first time it is impossible to know whether or not an anatomic obstruction exists. For this reason chemotherapy in conjunction with conservative treatment is to be recommended in all cases. Simpson presents the observations on 2 infants successfully treated with sulfadiazine. An initial dose of 0.5 Gm. of sulfadiazine was given, followed by 0.25 Gm. every four hours, with one dose at night. In 1 case an ointment containing 5 per cent of sulfathiazole was applied to the sinus openings. The additional conservative treatment consisted in cleansing the inferior meatus by suction, irrigation of the nasolacrimal duct with isotonic solution of sodium chloride and digital pressure on the distended lacrimal sac in an attempt to rupture a congenital membrane or stricture. From a survey of the literature on the use of sulfonamide drugs in ophthalmology it is evident that the use of sulfonamide compounds for congenital dacryocystitis has not received the attention it deserves. Too much emphasis has been placed on a physical obstruction as the underlying factor. Early employment of sulfonamide treatment in dacryocystitis may reduce the number of cases in which surgical treatment becomes necessary.

California and Western Medicine, San Francisco

61:281-324 (Dec.) 1944

Civilian Wartime Problems in Nutrition, from Standpoint of Physician. D. L. Wilbur.—p. 281.
Importance of Food in Wartime. A. J. Carlson.—p. 281.
California's Food Problem in Wartime Nutrition Program. A. J. Lorenz. —p. 285.
What Constitutes a Normal Diet. Grace G. Hardgrove.—p. 287.
How to Meet Needs of Normal Diet with Rationing of Food. Flora Rose.—p. 289.
Physician and OPA in Management of Patients Requiring Special Therapeutic Diets. E. T. Remmen.—p. 290.
Signs and Symptoms of Early Nutritional Deficiency. D. L. Wilbur. —p. 291.
Practical Use of Vitamins in Wartime. H. F. West.—p. 295.
Cooperative Endeavor Toward Nutrition in Industry. W. P. Lucas. —p. 297.
School Lunch Program. Ann P. Purdy.—p. 298.
Literature of Wartime Nutrition Movement. Ruth Okey.—p. 299.

Gastroenterology, Baltimore

3:435-544 (Dec,) 1944

Peptic Ulcer Problem in Army. J. E. Berk and A. W. Frediani.—p. 435.
*Prevention of Recurrence of "Peptic" Ulcer: Experimental Study. A. C. Ivy.—p. 443.
*Supradiaphragmatic Section of Vagus Nerves in Treatment of Duodenal and Gastric Ulcers. L. R. Dragstedt, W. L. Palmer, P. W. Schafer and P. C. Hodges.—p. 450.
Experiences with Peptic Ulcer in Army Station Hospital. L. Zetzel. —p. 472.
Observations on Chemical Composition of Blood and on Some Cardiovascular Reactions in Chronic Peptic Ulcer Throughout One Year. Helena E. Riggs, R. S. Boles, J. G. Reinhold and P. S. Shore.—p. 480.
Clinical Value of Functional Tests of Liver: Review, with Special Study of Plasma Prothrombin. J. Garrott Allen.—p. 490.
Gastroscopic Observations in Pyloric Obstruction. H. Scheff, J. L. Horner and B. Kenamore.—p. 506.
Flexirigid Gastroscope. L. L. Hardt.—p. 508.

Prevention of Recurrence of Gastric Ulcer.—Ivy applies the term enterogastrone to the chalone or hormonal agents which are responsible in part at least for the inhibition of gastric secretion and motility when an adequate concentration of fat or sugar is ingested. It is produced primarily in the upper intestine. Summarizing the evidence from animal experimentation, Ivy says that the parenteral administration of a mucosal extract of the upper intestine of swine prevents the occurrence of gastrojejunal ulcer in a high percentage of Mann-Williamson dogs. The protection afforded against ulcer is not limited to the period during which the extracts are being administered but has been observed to extend for periods as long as three years after cessation of treatment. Forty-three patients have to date received injections of enterogastrone. In 5 the injections were stopped because the patients complained of pain. Those selected for study had a long history of recurrences. Of the preparation the author is using 25 mg. as a canine inhibitory secretory unit. That is, 25 mg. given intravenously will reduce by 50 per cent the secretory response to 1 mg. of histamine dihydrochloride in a 20 pound (9 Kg.) dog with a pouch of the entire stomach. When given subcutaneously, 60 mg. constitutes a unit. Thus, when a human patient is injected subcutaneously with 200 mg., only approximately 3 units is given. This means that little depression of gastric secretion occurs. The direct control of acid secretion in man awaits the production of an enterogastrone preparation which contains less impurity than the present preparation. However, results obtained so far are encouraging. The 4 patients who received only enterogastrone therapy six times weekly for four months are now free from symptoms and of a duodenal niche, and the duodenal deformity has lessened in 2. Among 21 patients who had received injections three times weekly for seven to twelve months 4 have had one period of distress. The average expected recurrence of ulcer distress, on the basis of the past history, was reduced from 21 to 4 for a six months period. Several years of observation of more patients will be required to obtain reliable information on the late effects of the treatment.

Section of Vagus Nerves in Duodenal and Gastric Ulcers.—The presence of gastric secretory and motor fibers in the vagi and the large volume of experimental and clinical evidence indicating the crucial importance of gastric juice in the genesis of ulcer led Dragstedt and his associates to undertake complete division of the vagus nerves to the stomach in 11 cases of peptic ulcer. This was found to be most readily accomplished by opening the left pleural cavity, exposing the lower esophagus and isolating and dividing the vagus fibers before they pass through the diaphragm. The operation was well tolerated; there were no deaths, and the most serious complication was a postoperative pneumonia in 1 case. Gastrointestinal motility was not greatly altered, neither constipation nor diarrhea was produced, and it seems likely that food traversed the intestinal tract without great delay. Fluoroscopy after the operation revealed the persistence of peristalsis in the esophagus and the absence of cardiospasm, but in 1 case considerable atony in the wall of the fundus of the stomach was seen. No abnormalities in the motility or tonus of the small intestine could be determined. The continuous night secretion in most of the cases before operation was abundant. In 7 it exceeded a liter in twelve hours. This secretion was reduced

by the vagus section over 50 per cent in all cases and in many to a still greater degree. This provides final proof that the hypersecretion of gastric juice in cases of ulcer is neurogenic in origin and is probably due to a continuous hypertonus of the gastric secretory fibers in the vagus nerves. The striking relief of the ulcer pain and distress secured by the operation, the absence of untoward sequelae and the decrease in gastric secretion all indicate that this procedure will find a place in the treatment of many cases of intractable peptic ulcer. The first operation was performed only eighteen months ago and accordingly the time is still too short to pass judgment on the final result.

Journal of Clinical Endocrinology, Springfield, Ill.

4:517-566 (Nov.) 1944

Excretion of 17-Ketosteroids in Patients with Hyperthyroidism and Myxedema. W. W. Engstrom and H. L. Mason.—p. 517.

*Effect of Methyl Testosterone Treatment on Muscular Performance and Central Nervous System of Older Men. E. Simonson, W. M. Kearns and N. Enzer.—p. 528.

Tiselius Electrophoresis Studies of Plasma Proteins in Diabetes Mellitus. L. A. Lewis, R. W. Schneider and E. P. McCullagh, with technical assistance of J. Clark.—p. 535.

Limitations and Complications of Organotherapy in Male Homosexuality. S. J. Glass and R. H. Johnson.—p. 540.

Endocrine Diseases as Revealed by 13,000,000 Examinations of Registrants. L. G. Rowntree.—p. 545.

Effect of Methyl Testosterone on Performance of Older Men.—Simonson, Kearns and Enzer investigated whether exaggerated fatigue in older men might be partially due to reduction in sex hormone production. If this should be so, testosterone treatment might be expected to restore partially the working capacity. The 6 subjects on which the authors performed their tests varied in age between 48 and 67. All complained of excessive fatigability or loss of working capacity. The following tests were used: (*a*) endurance in a heavy type of dynamic work, leading to fatigue usually in not more than three minutes; (*b*) endurance in a type of static work; (*c*) absolute muscle force in several different muscle groups; (*d*) recovery of pulse rate after thirty knee bendings and during performance tests *a* and *b*; (*e*) maximum tapping rate; (*f*) fusion frequency of flicker. The fusion frequency may be looked on as an expression of the excitability of the retinocortical system and probably the whole central nervous system. Oral treatment with 30 to 40 mg. of methyl testosterone increased significantly, compared to a placebo period, the fusion frequency of flicker and back-muscle strength. The performance was increased in dynamic and static work in 4 of 5 subjects. No effect was noted on the strength of arm extensors and only a slight increase in handgrip strength in 2 of 6 subjects. The positive effect on the fusion frequency, back-muscle strength or dynamic work and static work performance was maintained up to eight months. A dosage of 20 mg. was sufficient to maintain the effect previously attained with 40 mg. in 1 subject and was insufficient in another. No effect was observed in maximum tapping rate and heart rate in exercise and recovery. The results appear to be compatible with the hypothesis that maintenance of a higher level of male sex hormone has an influence on the depression of working capacity with age.

Journal Industrial Hygiene & Toxicology, Baltimore

26:321-336 (Dec.) 1944

Carbon Monoxide Polycythemia. H. Brieger.—p. 321.

*Industrial Exposure to Butanol. I. R. Tabershaw, J. P. Fahy and J. B. Skinner.—p. 328.

Collection and Analysis of Halogenated Hydrocarbon Vapors Employing Silica Gel as Adsorbing Agent. C. Pernell.—p. 331.

"Dustshaker": Apparatus Designed for Production of Controlled Dust Concentrations in Air Breathed by Experimental Animals. W. B. Deichmann.—p. 334.

Industrial Exposure to Butanol.—Tabershaw and his associates have studied effects of butanol, used as a solvent and reactivator for synthetic resin such as polyvinyl butyral, a material used extensively in the manufacture of ponchos, rain coats and sleeping pads for military use. The manufacturing operations are performed for the most part by women. The garments are cemented together in sections. The butanol is used in two ways: 1. As a constituent of the cement it is usually mixed with other solvents, such as naphtha and ethyl alcohol. 2. As a reactivating agent, that is, when swabbed on the resin, it softens the material, permitting folding and sealing. The authors describe observations in six different plants using butanol. The chief complaint of the workers was irritation of the eyes. Air samples were taken in the areas where ocular irritation was most prevalent and it was determined that butanol concentrations above 50 parts per million produce eye irritation. As used in the manufacture of waterproofed products, the concentration of butanol rarely rises much above 100 parts per million, but in this range, while no serious systemic effects develop, ocular inflammation is common and serious enough to cause lost time and to disrupt operations. There was no evidence of toxemia, but the odor is disagreeable and produces in some workers a slight headache and vertigo. The vapors are also somewhat irritating to the nose and throat. Dermatitis is frequent. Gloves or mechanical devices were not used. An ointment seemed to offer some protection. The dermatitis consisted of a fissured eczema, especially around the finger nails and along the sides of the fingers. These lesions yielded rapidly to treatment and were prevented almost entirely by the use of a protective ointment before work and a lanolin emollient after work.

Journal of Infectious Diseases, Chicago

75:179-272 (Nov.-Dec.) 1944

Antimalarial Activity of Tyrothricin Against Plasmodium Gallinaceum. Lucy G. Taliaferro, F. Goulston and M. Silverman.—p. 179.

In Vitro Metabolism of Plasmodium Gallinaceum. M. Silverman, J. Ceithaml, L. G. Taliaferro and E. A. Evans.—p. 212.

Development of Plasmodium Gallinaceum from Sporozoite to Erythrocytic Trophozoite. C. G. Huff and F. Coulston.—p. 231.

Bacterial Destruction of Nicotinic Acid. S. A. Koser and Grace R. Baird.—p. 250.

Quantitative Relations Between Horse Hemoglobin and Antihemoglobin: Condition of Antigenicity. W. C. Boyd and S. Malkiel.—p. 262.

Experience with Slide Agglutination and Capillary Precipitin Methods for Typing Hemolytic Streptococci. Carolyn H. Hilles and M. Hamburger Jr.—p. 265.

Journal of International College of Surgeons, Chicago

7:423-508 (Nov.-Dec.) 1944

Treatment of Surgical Shock and Embolism. F. M. Allen.—p. 423.

Ulcerative Leiomyoma of Stomach. M. Behrend.—p. 436.

Ulcus Callosum Recti (Hochenegg). F. Mandl.—p. 447.

Intra-Abdominal Calcareous Tumors. E. S. Loup.—p. 452.

Muscle Reinnervation. H. E. Billig Jr.—p. 457.

Surgical Significance of Anatomic Layers of Gastrointestinal Tract. W. C. Burket.—p. 462.

Use of Preputium Skin in "Structive" Surgery. J. F. S. Esser.—p. 469.

Journal-Lancet, Minneapolis

65:1-36 (Jan.) 1945

Erythroblastosis Fetalis. E. M. Howard.—p. 1.

Detection of Pulmonary Tuberculosis on Induction into Military Service. D. L. Fink.—p. 5.

Indications for Surgical Treatment of Peptic Ulcer. C. G. Morlock.—p. 8.

Pregnancy and Diabetes. P. E. Ewald.—p. 13.

Dermatologic Problems in a College with A. S. T. P. Students. H. Sigel.—p. 15.

Higher Education in Postwar Era. R. Walters.—p. 17.

Anesthetic Aspiration Asphyxia as Cause of Maternal Mortality and Morbidity. M. Abramson.—p. 19.

Vision Problems of Military Students with Heavy Academic Loads. I Clark.—p. 23.

Hysterectomy: Selection of Appropriate Operation in Particular Case. V. S. Counseller and F. S. Sluder Jr.—p. 26.

Journal of Nervous and Mental Disease, New York

101:1-98 (Jan.) 1945

Peptic Ulcers in the Insane: Clinical and Postmortem Study. O. J. Pollak and F. Kreplick.—p. 1.

Ramsay Hunt Syndrome: Report of Case. N. R. Shulack and M. H. Kibbe.—p. 9.

Studies of Shock Therapy: Changes in Cerebrospinal Fluid Pressure Following Administration of Electric Shock Treatment (Preliminary Report). J. Negrin Jr.—p. 15.

Clinical and Electroencephalographic Studies: Electroencephalogram in Psychoneurotics. H. Strauss.—p. 19.

Study of Psychodynamics of Art Work of Nine Year Old Behavior Problem Boy. Margaret Naumburg.—p. 28.

A Schizophrenic's Knowledge of Himself. L. Kerschbaumer.—p. 65.

North Carolina Medical Journal, Winston-Salem

6:1-60 (Jan.) 1945

Planning for Mental Hygiene. G. H. Preston.—p. 1.
Present Status of Mental Health in North Carolina. M. H. Greenhill. —p. 7.
Proposed Program for State Hospital at Morganton. J. R. Saunders. —p. 22.
Coccidioidomycosis. J. P. McCracken.—p. 25.
Cesarean Section, with Special Reference to the Lower Uterine Segment Operations. W. Durwood Suggs.—p. 32.
*Favorable Response to Penicillin Therapy in Case of Treatment-Resistant Syphilis. R. O. Noojin, J. Lamar Callaway and A. H. Flower.—p. 34.

Penicillin in Treatment-Resistant Syphilis.—In the case reported by Noojin and his collaborators a penile syphilitic lesion developed in 1941 in a man aged 28. A serologic test for syphilis was said to be positive at this time, and treatment with neoarsphenamine was started. The patient received intravenous injections fairly regularly for the first ten injections, and treatment after this was intermittent. The penile lesion did not heal until three months after therapy was begun. During the next two and one-half years the patient received irregularly approximately sixty injections of neoarsphenamine and ten injections of bismuth subsalicylate. He was first seen at Duke Hospital on April 24, 1944 because of multiple ulcers over his hands and feet. During the six months preceding examination he had received an average of two intravenous injections of neoarsphenamine each month. Repeated Wassermann, Kahn, Kline and Mazzini tests on several blood specimens were strongly positive. Dark field examinations of several of the cutaneous lesions repeatedly revealed Treponema pallidum. The patient was given immediately bismuth subsalicylate 0.2 Gm. intramuscularly and mapharsen 0.06 Gm. intravenously. He was given a note to his physician with a request that the mapharsen be repeated within four days and that bismuth and mapharsen in the same dosage be given concomitantly each week for the succeeding six weeks. The patient returned ten weeks later. During this interval he had received concurrent intramuscular and intravenous therapy each week without improvement. The cutaneous lesions were again found by dark field examination to be positive for Treponema pallidum. The patient was now given 1,200,000 units of penicillin over a period of four days. Forty thousand units was administered intramuscularly every three hours, day and night, until a total of thirty injections had been given. Nineteen days after the final injection of penicillin, healing was complete and there were no new lesions.

Rocky Mountain Medical Journal, Denver

42:1-80 (Jan.) 1945

*Brucellosis in Goats: Recovery of Brucella Melitensis from Cheese Manufactured from Unpasteurized Goat's Milk. G. W. Stiles.—p. 18.
Problems in Management of Infections in Urinary Tract. H. L. Kretschmer.—p. 26.
Subacute Carbon Monoxide Poisoning with Cerebral Myelinopathy and Multiple Myocardial Necroses. K. T. Neubuerger and E. R. Clarke. —p. 29.
Neuroblastoma of Adrenal Medulla in Siblings: Case Report. H. J. Dodge and Miriam C. Benner.—p. 35.

Brucella Melitensis in Cheese from Goat's Milk.—According to Stiles the cheese manufactured from goat's milk in the vicinity of Trinidad, Colo., has an estimated annual value of a quarter of a million dollars. A sanitary survey of conditions on the goat ranches and the cheese making plants revealed insanitary practices and a polluted water supply. Brucella melitensis organisms were isolated from guinea pigs injected with goat cheese prepared from unpasteurized goat's milk. Of 19 cheese samples examined 8 proved to be positive for brucellosis. The testing of 14,339 blood samples, representing 131 herds, in the Bang's Disease Laboratory in Denver gave 8.5 per cent reactors. A man who appraised about 1,000 diseased goats contracted acute infection with clinical symptoms of brucellosis. Through the cooperation of the Colorado State Board of Livestock Commission the U. S. Public Health Service, the Food and Drug Administration and the Bureau of Animal Industry sanitary conditions have improved on goat ranches and in cheese plants. Reacting goats have been destroyed and newly acquired animals have been tested before being added to clean herds.

Surgery, Gynecology and Obstetrics, Chicago

80:1-112 (Jan.) 1945

War Casualties from Prolonged Exposure to Wet and Cold. R. H. Patterson and F. M. Anderson.—p. 1.
Simplified Design for Repair of Single Cleft Lips. J. B. Brown and F. McDowell.—p. 12.
*Superiority of Penicillin Over Bacteriophage, Sulfathiazole and Certain Other Antibacterial Substances as Indicated by Experimental Staphylococcal Infections in Chick Embryos. Helen Z. Jern and F. L. Meleney.—p. 27.
Experimental Studies of Peripheral Nerve Injuries: III. Study of Recovery of Function Following Repair by End to End Sutures and Nerve Grafts. L. Davis, G. Perret, F. Hiller and W. Carroll.—p. 35.
Spread of Uterine and Ovarian Carcinoma with Special Reference to Role of Fallopian Tube. R. C. Lynch and M. B. Dockerty.—p. 60.
*Effect of Continuous Caudal Analgesia on Uterine Motility During Labor: Study of 50 Patients with Lorand Tocogram. D. S. Frankel.—p. 66.
Pilonidal Cyst and Sinus, Their Management and Operative Treatment. W. Bartlett Jr.—p. 69.
Multiple Carcinomas of Large Intestine. H. Lewis Berson and L. Berger. —p. 75.
Further Studies on Preparation and Use of Sulfathiazole Ointment in Treatment of Burns. H. Perry Jenkins, J. G. Allen, F. M. Owens Jr., P. W. Schafer and L. R. Dragstedt.—p. 85.
Roentgenographic Interpretation of What Constitutes Adequate Reduction of Femoral Neck Fractures. R. T. McElvenny.—p. 97.
Supportive Immobilization of Cervical Spine. E. Boldrey.—p. 107.

Superiority of Penicillin Over Other Antibacterial Substances.—Jern and Meleny found that the inoculation of the chorioallantoic fluid of 10 day old chick embryos with 0.1 cc. of a savita broth culture of Staphylococcus aureus consistently brought about the death of the embryos within twenty-four hours. The administration of staphylococcus bacteriophage immediately following the inoculation of bacteria prolonged the life of all chick embryos. The cultures of the egg material of the phage-treated embryonated eggs resulted in a decrease and a degeneration of bacterial growth. A complete sterilization was seldom achieved. The presence of bacteriophage in the chorioallantoic fluid usually did not prevent the bacterial invasion of the blood stream of the embryos, although the appearance of phage in the blood usually could be demonstrated. Active multiplication of bacteriophage occurred in the majority of the cases when the undiluted or lower dilutions of phage were used. The in vitro experiments carried out with chorioallantoic fluid and with a mixture of the egg material showed that staphylococcus phage not only multiplied in these fluids but also produced a lysis of susceptible bacteria suspended in them. The presence of embryonic blood did not prevent bacterial lysis, although there was some inhibition. The administration of 100 units of the calcium salt of penicillin within six hours following the bacterial inoculation resulted in survival of the majority of the embryonated eggs. The therapeutic results were essentially the same when 10 units of penicillin was administered, but survivals fell off when 1 unit was used. The sterilization of the infected eggs, however, depended on the number of units of penicillin used. With 100 units of penicillin, 76 per cent of eggs were completely sterilized. The administration of sulfathiazole simultaneously with the bacteria failed to prolong the life of the embryonated eggs. Antistaphylococcus rabbit serum and staphylococcus antitoxin horse serum produced some prolongation of the life of the eggs, but the antibacterial effect of these substances was also insignificant. Carboxymethoxylamine produced a sterilizing effect in vivo and in vitro in a majority of the cases but was toxic for the embryos. Vioform was not toxic but possessed only a slight bacteriostatic effect. The new antibiotic agent from Bacillus T, a gram positive sporulating bacillus, exerted a significant protective effect, but it was not as efficient as penicillin.

Effect of Caudal Analgesia on Uterine Motility.—To determine more accurately the effect of caudal analgesia on the uterine contractions, Frankel studied the labors of 50 patients under caudal analgesia by means of the Lorand tocograph, an instrument devised for recording graphically the contractions of the uterus through the anterior abdominal wall. He found that the most important factor affecting uterine motility was the level to which the analgesia ascended. When the recommended level (between the sixth and tenth thoracic segments) was maintained, only 20 per cent showed a decrease in uterine motility, and these were minor changes. The remainder were unaffected. When the level of analgesia was permitted to ascend above the

fourth thoracic segment, labor was interrupted in 69 per cent of the patients. When a low level of analgesia involving only the sacral nerves was achieved in 2 patients there was a great improvement in the strength and frequency of the uterine contractions. This improvement continued after relief from pain was attained. Forty-four per cent of patients studied showed a progressive decrease in uterine tone. This did not appear related to the level of analgesia.

United States Naval Med. Bulletin, Washington, D. C.

44:1-224 (Jan.) 1945

Studies on Filariasis in Samoan Area. E. E. Byrd, L. S. St. Amant and L. Bromberg.—p. 1.
Filariasis in Returning Marines. F. Glauser.—p. 21.
*Clinicopathologic Study of Early Filariasis with Lymph Node Biopsies. S. S. Zuckerman and J. S. Hibbard.—p. 27.
Preliminary Revision of Scutellaris Group of Genus Aedes. D. S. Farner and R. M. Bohart.—p. 37.
Our Leprosy Problem. G. M. Saunders.—p. 54.
Intestinal Parasitic Infections in Naval Hospital in New Zealand. E. K. Markell.—p. 65.
Psychogenic "Malaria." B. R. Merrill.—p. 69.
Study of 1,063 Naval Offenders. B. Locke, A. C. Cornsweet, W. Bromberg and A. A. Apuzzo.—p. 73.
Treatment of Intestinal Obstruction in Field and Aboard Ship. J. S. Hibbard.—p. 87.
Medical Problems on Attack Transport. J. B. Oliver, A. C. Kelly and R. P. Watkins.—p. 92.
Hearing Tests: Evaluation. C. W. Shilling, I. A. Everley and J. D. Harris.—p. 100.
Hearing Aids. J. C. Howard Jr.—p. 117.
Simplified Technic for Acrylic Jackets. L. H. Dahl.—p. 121.
Biostatistics in Medical Research: II. Probabilities in Small Samples. H. M. C. Luykx.—p. 125.
Kodachrome Photomicrography in Malaria: Rapid Method of Instruction. H. M. Maveety, R. B. Turnbull Jr. and C. R. Bauer.—p. 134.
*Plasma Treatment of Mumps Orchitis: Report of 5 Cases. R. G. Smith. —p. 159.

Early Filariasis.—After reviewing the clinical course in a large series of filariasis patients in Samoa it became apparent to Zuckerman and Hibbard that although the majority of patients usually showed classic signs and symptoms of retrograde lymphangitis there remained a small number of patients with a minimal degree of disability. It was determined that an absolute diagnosis of filariasis could not be made without a careful clinical correlation unless the parasite was present in the tissue. Lymph node sections were restudied with the object of establishing, if possible, the relationship between the signs and symptoms observed in the early cases and the microscopic changes manifested in the nodes. Lymph node biopsies were done on 62 patients, representing various stages of the disease. Although a few nodes measured as much as 2.5 cm. in length the majority varied from 0.7 to 1.5 cm. They were elongated and discrete, and the overlying skin was freely movable. Generally they were set in a fine, fibrous periglandular network which allowed a clean line of cleavage on sharp dissection. On cross section the nodes were firm and homogeneous, the capsule thickened and often edematous and fibrosed. A coiled male or female adult worm cut in cross or sagittal section was the characteristic picture in the lymphatic channels. The parasite lay in a granulating lymph channel which was surrounded by epithelioid cells, Langhans giant cells, plasma cells and a dense infiltration of eosinophils. The endothelium of the lymph channels exhibited a granulomatous hyperplasia, with swelling of the cells. Some lymphatic channels showed endothelial changes and obliteration, other channels obliterative endolymphangitis with adventitial fibrosis. In the lymph node biopsies the authors differentiate four different variations. In the first group adult filarias were found in or outside the lymph node, in the second group dense eosinophilic infiltration was present but adult filarias were absent, in the third group both adult worms and eosinophilic infiltration were absent from the biopsy tissue and in the fourth group there were neither adult worms nor eosinophils. The authors believe that infection by Wuchereria bancrofti is accompanied by a generalized disturbance of the reticuloendothelial system which manifests itself as a hyperplasia of these cells. The endothelium of the lymph channels is similarly affected and the end result is an obliterative endolymphangitis. Eosinophilia is due to the presence of a parasite, usually the result of a dying parasite. The plugging of the lymphatic channel by the parasite causes backing up of toxic products, which would account for the so-called retrograde lymphangitis. Biopsy is unnecessary for diagnosis in the majority of cases but is useful as confirmatory evidence in the clinically atypical cases.

Plasma Treatment of Mumps Orchitis.—Smith says that an outbreak of 40 cases of mumps occurred aboard ship. Five of the patients developed orchitis. All patients were given 500 cc. of reactivated dried pooled plasma. Results obtained were excellent to dramatic. Four patients volunteered the information that the plasma gave them quick relief. Not enough time has elapsed to determine if any patients will develop atrophy of the testes. One patient received a second 500 cc. of plasma when meningitic signs and symptoms appeared.

War Medicine, Chicago

7:1-70 (Jan.) 1945

Medical Aspects of Rehabilitation of Persons with Tuberculosis. H. E. Hilleboe.—p. 1.
Cause, Effect and Treatment of Air Blast Injuries. R. E. Tunbridge. —p. 3.
Clinical Malaria in Wartime. F. R. Dieuaide.—p. 7.
Relationship of Stress, Breakdown, Instability and Recovery in Men with Combat and with Noncombat Neuroses. R. S. Schwab and H. Rochester.—p. 12.
Relapsing Fever in Panama: Report of 6 Cases. A. G. Cohen.—p. 19.
*Effect of Morphine Sulfate on Persons Exposed to Simulated Altitude. * E. W. Peterson, M. B. Bornstein and H. H. Jasper.—p. 23.
*Effect of Sulfathiazole on Persons Subjected to Simulated Altitude. E. W. Peterson, M. B. Bornstein and H. H. Jasper.—p. 29.
Rehabilitation of War Casualties. J. B. Dynes.—p. 32.

Effect of Morphine Sulfate at High Altitudes.—Peterson and his associates point out that the sick or wounded persons who are candidates for transport by air should receive morphine for the control of pain or shock. In such persons it becomes a matter of concern whether the effects of morphine on the body, other than those of analgesia and sedation, may seriously impair their ability to undergo air transport. The authors exposed 9 subjects to simulated altitude in decompression studies to determine the effect of morphine sulfate on their ability to withstand the physiologic effects of anoxia. They found that when the reflex excitability of the nervous system is at a reasonably high level morphine sulfate in a ¼ grain dose (15 mg.) does not alter the average blood oxygen saturation under conditions of simulated altitude. The ability to respond to oxygen administration was unhampered. When the reflex excitability of the nervous system was not maintained following morphine sulfate, as occurred in 2 subjects, there was a deterioration in the blood oxygen saturating ability under conditions of simulated altitude. However, the ability to respond to oxygen administration was unhampered. No significant deviation of the electrocardiogram or pulse rate occurred when anoxia was combined with morphine.

Effect of Sulfathiazole at High Altitudes.—Peterson and his co-workers made studies on the effects of sulfonamides on altitude tolerance in 3 men. Normal adult males, receiving sulfathiazole in full therapeutic doses, failed to show significant deviations in blood oxygen saturation levels, electrocardiograms or electroencephalograms when subjected to simulated altitudes of 20,000 feet. Anoxia produced in the decompression chamber at simulated altitudes of 20,000 feet failed to change in a significant manner the subjective reactions of human subjects to full therapeutic doses of sulfathiazole. It is concluded that the evidence does not contraindicate the use of this drug for wounded personnel who are to be transported below or above 10,000 feet with supplementary oxygen.

West Virginia Medical Journal, Charleston

41:1-32 (Jan.) 1945

Health: Public Responsibility. J. M. Broughton.—p. 1.
Transurethral Resection. C. A. Hoffman.—p. 4.
Recent Advances in Treatment of Purulent Meningitis. W. W. Waddell Jr.—p. 6.
Use of Sulfamerazine in Pneumonia. G. P. Heffner.—p. 12.

41:33-64 (Feb.) 1945

Surgical Experience in Continental Naval Hospital. J. O. Rankin. —p. 33.
Artificial Penis. B. S. Brake.—p. 45.
Shoulder Presentation with Prolapse of Hand. J. C. Arnett.—p. 47.
Cesarean Section: An Analysis of 1,088 Consecutive Cases. S. G. Kohn, J. H. Morrison and L. H. Douglass.—p. 49.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

19:147-184 (Dec.) 1944

Macrocytic Anemia in Children, with Report of 3 Cases Showing Megaloblastic Erythropoiesis. L. J. Davis.—p. 147.

Refractory Anemia (Fanconi Type): Its Incidence in 3 Members of One Family, with in 1 Case a Relationship to Chronic Hemolytic Anemia with Nocturnal Hemoglobinuria (Marchiafava-Micheli Disease or Nocturnal Hemoglobinuria). J. V. Dacie and A. Gilpin.—p. 135.

Erythroblastic Anemia with Bone Changes in Egyptian Children. Possible Cooley's Type. M. Diwani.—p. 163.

Observations on Urine of Newborn Infant. J. Thomson.—p. 169.

Myocarditis in Acute Infective Diseases: Review of 200 Cases. C. Neubauer.—p. 178.

Australian and New Zealand J. Surgery, Sydney

14:75-144 (Oct.) 1944

Practical Points in Plaster Technic: Two Years of Experience in Forward Surgery with Royal Army Medical Corps (Mobile) Casualty Clearing Station, 1941-1943. L. S. Rogers.—p. 75.

*Immediate and Late Treatment of Arteriovenous Fistula. E. Holman.—p. 82.

*Report of 40 Cases of Gunshot Wounds of Chest Treated at Base Hospital. C. H. Horsley.—p. 91.

Traumatic Rupture of Urethra and Bladder. H. C. Barry.—p. 104.

Method of Treatment of Compound Fractures of Humerus. G. Godfrey.—p. 114.

Progressive Bacterial Synergistic Gangrene, with Report of Case. N. J. Bonnin.—p. 119.

Treatment of an Arteriovenous Fistula.—Simple ligation of the artery proximal to an arteriovenous fistula, such as might be done proximal to a simple aneurysm, is contraindicated, Holman says. It is obvious that the blood flowing through the collateral vessels would flow back to the heart through the site of the lessened resistance at the fistula, thus bypassing the peripheral vascular bed. Gangrene would be inevitable under these conditions. The operation of choice for an arteriovenous fistula is quadruple ligation of artery and vein proximal and distal to the fistula, with excision of the abnormal communication. A fistula which has been allowed to remain four months or longer has usually so stimulated collateral circulation that ligation of the main artery to a limb can be performed with impunity. If excision of the fistula is impossible owing to difficulty in mobilization because of excessive scarring or because of the inclusion of main nerve trunk in dense scarring surrounding the fistula, quadruple ligation without excision may be preferable. The proximal artery, however, must be sufficiently mobilized to permit ligation at two points and division between them. Ligation in continuity may lead to reestablishment of the arterial lumen and reactivation of the fistula. The success of operations on the large vessels depends in great measure on the avoidance of sepsis. The strictest precautions against infection must be followed throughout, and the liberal use of the sulfonamides locally and systemically is indicated in any contaminated or potentially infected wounds. In surgery of the large vessels to pack or to drain wounds is to invite almost certain disaster. If there is any question of infection, penicillin should be promptly administered in maximum dosage.

Gunshot Wounds of Chest.—Horsley reviews 40 gunshot wounds of the chest treated at an Australian general hospital. The patients were admitted over a period of three months and their stay in the hospital exceeded seven days. The treatment was almost entirely conservative. A small intrapulmonary metallic foreign body causes little morbidity, and there appeared to be no definite indication for its removal. An intrapleural foreign body, on the other hand, appears to be a potent source of empyema, particularly when the foreign body is thick and jagged. Rapid cure of the pleural infection followed removal of such foreign bodies. Foreign bodies in the chest wall are frequently removed. Perforating wounds resulting from a small caliber bullet seem to cause severe morbidity only when they produce bronchopleural fistulas. Of the perforating chest wounds 25 per cent developed a bronchopleural fistula, which was the most difficult of all complications. Pleural effusion was present in the majority of the cases, and the presence of hemothorax played a prominent part. Infection was not a serious complication. Hemoptysis was of not much value as an indication either of the nature of the wound or of the degree of morbidity to be expected. The object of the treatment was to close the thorax, remove effusion, establish a negative pressure in the pleural cavity and, if necessary, remove any foreign body from the pleural cavity. Once a "dry" pleural cavity and an expanding lung were obtained, full expansion of the thorax was encouraged by lung exercises and physical training. Blood transfusion was given to debilitated patients. The chief indication for intercostal drainage was the presence of recurring exudate requiring frequent aspiration. An attempt was made in every case to combine the use of an intercostal tube with negative pressure drainage. Thoracotomy was performed in two types of conditions: (*a*) retained intrapleural foreign body and (*b*) gross pleural infection which failed to respond to intercostal drainage.

British Journal of Radiology, London

17:355-386 (Dec.) 1944

Further Observations on Lung Disease in Boiler Scalers. L. Dunner and R. Hermon.—p. 355.

Energy Absorption: III. The Mathematical Theory of Integral Dose and Its Applications in Practice. W. V. Mayneord.—p. 359.

Serial Roentgenograms of Chest in Periarteritis Nodosa as Aid to Diagnosis, with Notes on Pathology of Pulmonary Lesions. A. Elkeles and L. E. Glynn.—p. 368.

Action of Neutrons on Developing Rat Retina. F. G. Spear and Katharine Tansley.—p. 374.

Case of Bronchial Carcinoma Presenting Diagnostic Difficulties. R. B. Guyer.—p. 380.

Unusual Case of Joint Disease (A Possible Example of Arthritis Psoriatica). H. Jungmann and V. S. Stern.—p. 383.

Cystic Disease in an Azygos Lobe with Phrenic Nerve Paresis. G. F. Rees-Jones.—p. 368.

British Medical Journal, London

2:745-780 (Dec. 9) 1944

Treatment of Hyperthyroidism with Thiouracil. A. M. Nussey.—p. 745.

Hemoglobin Level in Municipal School Children: Effect of Iron Therapy, School Dinners, and Season. R. H. Dobbs, Helen M. M. Mackay and K. Bingham.—p. 748.

Dietary Control of Alloxan Diabetes in Rats. J. H. Burn, T. H. C. Lewis and F. D. Kelsey.—p. 752.

Antibacterial Action of 2-Aminophenol (O-Aminophenol). Mary Barber and G. A. D. Haslewood.—p. 754.

Mediastinal Teratoma Successfully Removed by Operation. A. W. Fawcett.—p. 755.

2:781-806 (Dec. 16) 1944

Smallpox Vaccination by Multiple Pressure Method. H. J. Parish.—p. 781.

Two Stage Method of Treatment in Diabetes. R. H. Micks.—p. 784.

Some Aspects of Gonorrhea in Navy. S. Matthews and F. G. Beilby.—p. 787.

Treatment of Wounds by Delayed Suture. W. Patrick.—p. 788.

Origin of Bronchogenic Tuberculosis in Adult: Pathologic Aspects of "Exogenous and Endogenous Reinfection." W. Pagel.—p. 791.

2:807-840 (Dec. 23) 1944

Supply of Bodies for Dissection: Historical Review. N. M. Goodman.—p. 807.

Estimation of Heat Radiation in Clinical Practice. D. S. Evans and K. Mendelssohn.—p. 811.

Radical Operation for Varicose Veins. H. Dodd.—p. 814.

Sulfonamide Allergy: Persistence of Desensitization. R. G. Park.—p. 816.

Penicillin in Civilian Practice. H. B. May.—p. 817.

Journal of Physiology, London

103:253-358 (Dec. 15) 1944

Investigations on Muscle Atrophies Arising From Disuse and Tenotomy. J. C. Eccles.—p. 253.

Absolute Muscle Force in Ankle Flexors of Man. H. A. Haxton.—p. 267.

Acid Labile CO_2 in Mammalian Muscle and p_H of Muscle Fiber. E. J. Conway and P. J. Fearon.—p. 274.

Action of Adrenalin and of Choline Esters on Uterus of Sheep. J. A. Gunn.—p. 290.

Liberation of Histamine During Reactive Hyperemia and Muscle Contraction in Man. G. V. Anrep, G. S. Barsoum, S. Salama and Z. Souidan.—p. 297.

Emulsification of Fat in Intestine of Rat and Its Relationship to Absorption. A. C. Frazer, J. H. Schulman and H. C. Stewart.—p. 306.

Observations on Some Conditions Affecting Rate of Hormone Output by Suprarenal Cortex. Marthe Vogt.—p. 317.

Inhibition of Histamine Release by Pituitary-Adrenal Mechanism. G. Ungar.—p. 333.

Optical Method for Recording Peripheral Blood Pressures and Pulse Rates in Unanesthetized and in Anesthetized Rabbits. C. B. B. Downman, C. C. MacKenzie and B. A. McSwiney.—p. 344.

Effects of Acute Hemorrhage on Peripheral Blood Pressure in Unanesthetized and in Anesthetized Rabbits. C. B. B. Downman, C. C. MacKenzie and B. A. McSwiney.—p. 350.

Lancet, London

2:775-808 (Dec. 16) 1944

Inhalation of Chemotherapeutic Substances. N. Mutch.—p. 775.
*Infective Dermatoses Treated with Penicillin. P. H. Taylor and K. E. A. Hughes.—p. 780.
Nomogram for Correcting Sahli Hemoglobinometer Readings. G. H. Bell and Mary L. McNaught.—p. 784.
Prognosis After Successful Pneumonectomy. J. M. Cheale.—p. 784.
Pregnancy After Pulmonary Lobectomy. A. G. Bryce and Eleanor M. Mills.—p. 786.

Penicillin in Infective Dermatoses.—At a large military hospital Taylor and Hughes used penicillin in the treatment of sycosis barbae, impetigo contagiosa, furunculosis and other varieties of the large group of eruptions known as the infective dermatoses. Penicillin was applied locally in various ways in an endeavor to find the most efficient and most economical mode of application. The preparations tried included crude penicillin filtrate in a base of equal parts of lanette wax, liquid petrolatum and water; calcium penicillin in a base of 30 per cent lanette wax in water; sodium penicillin in a base of 30 per cent of lanette wax; sodium penicillin in aqueous solution; penicillium mold of about fourteen days' growth, and penicillium mold crushed up in a base of 30 per cent lanette wax in water. Before treatment the lesions were examined bacteriologically. Cultures on blood agar were made with a wool swab. The plates were incubated for twenty-four hours or longer, the organisms growing were identified and a rough colony count was made. All organisms grown were tested for sensitivity to penicillin, and all staphylococci had their coagulase production assessed. During treatment, daily cultures were made in a similar way. The authors found that penicillin is effective in the local treatment of certain skin diseases caused by cocci. The most satisfactory method of treatment of sycosis barbae and impetigo is to spray the lesions with an aqueous solution containing 200 units of penicillin in each cubic centimeter. An adequate dose of penicillin from the start is essential to prevent the development of penicillin-fast organisms. A strength of 200 units of penicillin in each cubic centimeter or 400 units per gram of lanette base seems to be sufficient. The pain in deep-seated lesions (furuncles) is much relieved after application of penicillin. An underlying seborrheic state in cases of sycosis and impetigo is liable to cause relapse soon after cessation of treatment and necessitates further courses of treatment. The appearance of penicillin-insensitive organisms indicates that further treatment with penicillin is of little value.

2:809-840 (Dec. 23) 1944

*Traumatic Uremia: Reports on Eight Cases: E. M. Darmady, A. H. M. Siddons, T. C. Corson, C. D. Langton, Z. Vitek, A. W. Badenoch and J. C. Scott.—p. 809.
*Deficiency Bowel Pattern in Polish Refugees, African and Indian Adults and Children (Kwashiorkor). J. S. Brown and H. C. Trowell.—p. 812.
Better Drainage for Nontuberculous Empyema. A. K. Henry.—p. 816.
Congenital Subluxation of Acromioclavicular Joint. J. Grieve.—p. 817.
Fluorescence Microscopy in Detection of Tubercle Bacilli. H. Lempert.—p. 818.
Delayed Rupture of Spleen. L. Gillis.—p. 822.
Autograft of Amputated Thumb. S. Gordon.—p. 823.
Septicemia Due to Bacterium Necrophorum and an Anaerobic Streptococcus. H. P. Jones.—p. 824.

Traumatic Uremia.—Darmady and his associates report 6 cases of uremia occurring in young soldiers a few days after they were wounded by high explosive missiles. The injuries were severe but did not seem sufficient to cause death. All the men developed oliguria, vomiting and an elevated blood urea. In searching for a causative factor the following features were noted: 1. The injuries in all cases were caused by high explosives. 2. There were considerable injuries to the extremities in all cases; in none was there a crushing injury, nor was the local condition in itself sufficient to account for death. 3. Low blood pressure was recorded at some stage in 5 cases. 4. There was a lesion of a major vessel in 6 cases. 5. Sulfanilamide was given by mouth in 5 cases. 6. All the men were given transfusions of group O blood. No clinical evidence of mismatched transfusion was apparent. Cases have been reported during the present war under the title of "crush syndrome" in which the clinical picture and postmortem findings in the kidneys are comparable to those found in these 6 cases. More recently it has been pointed out that similar changes are sometimes found in injuries without crushing, including head injuries and also in association with blackwater fever, pyloric stenosis with vomiting, and septic abortion. While not all the biochemical and renal changes associated with all these conditions are identical, there is sufficient similarity to justify a search for a common etiologic basis. The mechanism which leads to the sequence of events is unknown. There seem to be two possible explanations: (1) a metabolic product carried to the kidney by the blood stream and (2) anoxia of the kidney resulting either from a period of hypotension or from a neurogenic vascular disturbance.

Deficiency Bowel Pattern.—Brown and Trowell describe experiences in diagnosing and treating a malnutritional state which in its advanced stage is often seen in African adults and children (kwashiorkor). Apathy of the facies is exaggerated by the mild edema, which obscures the expression. The patient is mentally dull, is sluggish in his movements and appears depressed. The hair is scanty. The characteristic dermatosis consists of scaly shiny dark brown areas appearing over the pressure sites of the back and buttocks or anywhere. The keratin layers of the skin of the legs become thin and shining, and fissure and crack. The dermatosis becomes moist, resembling intertrigo and peels to reveal pale areas. Cheilosis may develop. The patient complains of a variety of gastrointestinal symptoms. A few have sore mouth with loss of lingual papillae, and fissures appear in a raw red tongue. Stomatitis is common. Anorexia may be severe and twisting; burning abdominal pains are often reported. Loose stools are common; they are bulky, frothy and acid. They contain much undigested starch and muscle fibers. Flagellates, mainly Giardia intestinalis, are common. Much flatus is passed by rectum. Advanced cases show distended coils of intestine, and peristalsis is usually painful. Sigmoidoscopy may show a congested or granular mucosa. Paresthesias are common in the hands and feet, and slight peripheral neuritis is present in many cases. Anemia does not respond readily to iron or liver administered orally. Most patients had a history of inadequate diet over a long period; their meals had consisted mainly of cooked carbohydrate and were deficient in calories, animal protein, fat, green vegetables and vitamins. Patients did not improve when given an adequate diet; it was necessary to add vitamin concentrates. Early cases responded well to supplements of cooked liver or brewers' yeast given daily. More advanced cases did not respond to oral therapy but showed improvement after large doses of crude liver extracts, given parenterally. Advanced cases, especially if complicated by infections, did not respond to treatment. These patients either died or became chronic invalids. In untreated cases the prognosis is uniformly bad. Almost all progress rapidly to death in a few weeks or months.

Medical Journal of Australia, Sydney

2:525-556 (Nov. 18) 1944

Mite Borne (Scrub) Typhus in Papua and Mandated Territory of New Guinea: Report of 626 Cases. S. W. Williams, A. J. M. Sinclair and A. V. Jackson.—p. 525.
Observations on Epidemiology of Scrub Typhus. C. E. Cook.—p. 539.
Notes on Habits and Distribution of Trombiculid Mites in Queensland and New Guinea. R. N. McCulloch.—p. 543.

Archivos Argentinos de Pediatria, Buenos Aires

15:289-382 (Oct.) 1944. **Partial Index**

*Familial Spasmodic Paraplegia. E. Cienfuegos and J. Daneri N.—p. 189.

Familial Spasmodic Paraplegia.—Cienfuegos and Daneri report 3 cases of familial spasmodic paraplegia of the Strümpell-Lorrain type in brothers aged 8, 13 and 15 years. The father and 3 sisters aged 2, 4 and 7 years are normal. The mother is nervous but otherwise normal. The patients presented a normal physical and mental development up to the age of 8 months or 1 year, when they showed symptoms of the disease. Papillary atrophy, oligophrenia, speech disorders and abnormal reflexes were encountered in all. The authors discuss the differential diagnosis between familial spasmodic paraplegia of the Strümpell-Lorrain type, the group of familial or individual spasmodic forms of paraplegia, the familial amaurotic idiocy type (the Tay-Sachs disease) and other forms of diffuse

periaxial encephalitis. They conclude that all of these manifestations are different forms of spinocerebellar degeneration. The type of the disease depends on the acuteness and extent of nervous degeneration.

Revista Argentina de Neurol. y Psiquiat., Rosario

9:185-280 (June) 1944. **Partial Index**

*Progressive Lenticular Neurohepatic Degeneration (Wilson's Disease) and Pseudosclerosis. T. Fracassi.—p. 185.

Progressive Lenticular Neurohepatic Degeneration.—Fracassi reports 1 case of chronic and 1 case of acute hepatolenticular degeneration of unknown etiology. The clinical symptoms of the acute form were those of choreic extrapyramidal hyperkinesis and those of the chronic case of parkinsonian rigidity and tremors. The cerebral lesions were similar in severity but not in extent. In both cases the lesions were distributed mostly over the medial part of the striated body and especially over the putamen, but there were also large spongy lesions in the deeper layers of the cerebral cortex, the red nucleus, the white matter and the dentate nucleus in the cerebellum, with small necrotic perivascular foci. There were also glial changes. The clear glial nuclei were enlarged and had assumed several shapes: oval, lobulated and elongated. The chromatin network had disappeared from the glia, giving it a colorless appearance. The protoplasm of the glial cells contained some granules of metachromatic pigments. The changes in the liver were those of atrophic cirrhosis of the Laënnec type in the chronic case and of insular cirrhosis in the acute case. Pathologic findings suggest that the disease is a form of a diffuse degeneration and demyelization of the cerebrum, the cerebellum, the red nuclei, the dentate nuclei and the white matter of the cerebellum, rather than a lesion of the putamen and the striated body.

Klinische Wochenschrift, Berlin

22:329-352 (May 1) 1943

Problems of Internal Secretion. H. Marx.—p. 329.
*Treatment of Diphtheria Patients with Homologous Serum. F. von Bormann, L. Schall and E. Kirschhöfer.—p. 332.
Etiology of Infectious Pneumonias in White Mice and Their Relations to Etiology of Human Influenza. W. O. Gross.—p. 335.
Gastrointestinal Diseases and Avitaminosis B_1. O. Carere-Comes.—p. 339.
*Pathogenesis of Polycythemia Vera (Castle's Experiment). R. Stöger.—p. 342.
Problem of Prophylaxis and of Treatment with Heparin ("Liquemin") for Postoperative Thromboembolism. R. and G. Reimann-Hunziker.—p. 344.
Effect of Acid and Alkali Diet on Various Functions of Skin. Charlotte Umrath.—p. 346.

Homologous Serum Therapy in Diphtheria.—Bormann and his associates report observations in 16 cases of diphtheria treated with human antitoxin serum. Continuous examination of the antitoxin content of the blood of these patients revealed a pronounced increase in the antitoxin level of 10 of the patients during the second week in addition to the increase in the antitoxin level immediately after the administration of the serum. The new antitoxin titer did not change during an investigation period of from six to eight weeks. In 6 of the cases treated with human antitoxin serum and in 2 cases treated with horse serum the antitoxin level of the blood decreased slowly after the initial increase, but active antitoxin formation by the human organism was likewise suggested at least in 1 of the cases treated with horse serum, since for six weeks the antitoxin level remained considerably above the protection threshold. These observations suggest that serum administration to diphtheria patients does not interfere with the active formation of antibodies. That applies to the very early administration as well as to repeated administration. It seems likely that during the first days the antigen stimulus may appear, which represents the eliciting cause of the later active antitoxin formation. The antigen stimulus thus arises at the time when it cannot as yet be prevented by the passive administration of antitoxins. Toxic diphtheria occurred in children in spite of previous active immunization, but the mortality of the immunized children was lower, amounting to 29.2 per cent as compared to that of 85.5 per cent of the nonimmunized children. In cases of toxic diphtheria the fatal intoxication of the organism occurs during the first hours of the disease in spite of the serum therapy.

Pathogenesis of Polycythemia Vera.—Stöger's concept of Vasquez's disease is that it is due to an abnormal increase in the intrinsic factor in the presence of a diathesis characterized by a deficiency in the central regulation of hemopoiesis. Castle's experiment was repeated as follows: An untreated fasting patient with pernicious anemia was given a broth consisting of 200 Gm. of lean beef meat and 75 cc. of incubated gastric juice secreted by a fasting normal man after histamine administration. In a second experiment the untreated patient with pernicious anemia was given a broth consisting of 200 Gm. of lean beef meat and 75 cc. of incubated gastric juice secreted by a fasting patient with Vasquez's disease after histamine administration. The continuous control for eight days of the reticulocytes, the erythrocytes and the hemoglobin revealed a stronger reaction in the second experiment than in the first. The increase in the number of reticulocytes in the second experiment was more than double when compared with the increase in the number of reticulocytes in the first experiment. The number of erythrocytes was increased from 1,080,000 to 1,740,000 in the second experiment, whereas almost no increase occurred in the first experiment. There was also an increase in the hemoglobin content in the second experiment. After an interval of ten days a third experiment was carried out by repeating the first on the same patient except for the administration of the gastric juice secreted by a different normal person. The results were the same as in the first experiment. It is suggested that a more than normal increase in the intrinsic factor has been demonstrated since an extraordinary increase in the number of reticulocytes resulted under the same experimental conditions from the administration of the same amount of gastric juice and of the same amount of extrinsic factor.

Acta Medica Scandinavica, Stockholm

113:267-372 (March 18) 1943

Atypical Tuberculosis-Boeck's Sarcoid. R. Opsahl.—p. 267.
*Occurrence of Thrombosis and Pulmonary Embolism in Pneumonia. E. Ask-Upmark.—p. 286.
Experiments with Transfusion of Infectious Mononucleosis to Man. J. Bang.—p. 304.
A Case of Transient Pulmonary Infiltration with Eosinophilia, with Fatal Issue After Treatment with Epinephrine Spray for Asthma. O. J. Broch.—p. 311.
Occurrence of Human Intestinal Protozoa in Norway. J. Boe.—p. 321.
Joint Disorders Associated with Toxic Diffuse Goiter. E. Snorrason.—p. 329.
Iron Content of Serum in Patients with Hemorrhagic Anemia. K. Brochner-Mortensen.—p. 345.
Serum Iron in Patients with Hyperchromic Anemia in Idiopathic Steatorrhea. K. Brochner-Mortensen.—p. 362.

Thrombosis and Pulmonary Embolism in Pneumonia.—Ask-Upmark analyzed 1,454 cases of lobar pneumonia treated at the Medical Clinic in Lund from 1916 to 1941. Thromboembolism was observed in 27 instances, i. e. in about every 50th case. There were 11 instances in men and 16 in women. Persons over 40 years of age were affected somewhat more often than those below this age. Thus 10 of the 27 patients with thromboembolism were less than 40 and 17 persons were over 40. During the last four years (1938 to 1941) more instances of thromboembolism have been recorded than during the preceding twenty-two years owing to the introduction of specific therapies such as serum therapy, chemotherapy or both, which allow patients to survive and to develop thromboembolism who previously would have succumbed to the disease at an early stage. The average time elapsed between the onset of pneumonia and the onset of thromboembolism was thirteen days, the average time elapsed between the crisis and the onset of thromboembolism eight days. The evolution of thromboembolism should be anticipated when the temperature does not reach the normal level after the crisis or lysis, although it may occur even if this level is reached. Hemodynamic factors favoring the development of thromboembolism are the reduction of muscular tonus, the impairment of the blood pressure and the involvement of the heart. Hematologic factors are venous stasis, increase in the thrombocytes and in particular the behavior of the thrombin. The concept is suggested that an important feature in the pathogenesis of thromboembolism is the impairment caused by the pneumonic process of the basophil parenchyma, the heparin-producing mast cells.

Book Notices

Physical Medicine in General Practice. By William Bierman, M.D., Attending Physical Therapist, Mount Sinai Hospital, New York. Cloth. Price, $7.50. Pp. 654, with 310 illustrations. New York & London: Paul B. Hoeber, Inc., 1944.

This book has been prepared primarily for the general practitioner. It contains descriptions of many procedures. The section on hydrotherapy includes descriptions of the steps in the application of the various types of wet compresses and packs to the body. The simple types of whirlpool baths that can be used in the office and in the hospital are described. The section on infra-red irradiation contains a brief description of the physics of radiant energy and the use of luminous bakers, heat lamps and cabinet baths. The limitations and lack of practicability of the cabinet baths are not emphasized. Only the long wave or conventional diathermy is discussed in the chapter on diathermy. The author uses the term "short wave currents" instead of the commonly used term "short wave diathermy" in discussing the high frequency currents produced by vacuum tube oscillators. The effective and practical technics of applications of condenser pads and induction coils to the various regions of the body are pictured and described. In the chapter on fever therapy the author discusses many of the early methods that were used for induction of artificial fever as well as the technics commonly used today. The indications for and dangers of fever therapy are presented. However, this section does not emphasize adequately the dangers of fever therapy when carried out by inexperienced persons and without adequate equipment. The section on the galvanic current includes a discussion of the use of low voltage currents for iontophoresis, muscle stimulation, electrolysis and testing for reaction of degeneration. The use of the faradic and the sinusoidal currents is considered briefly. A brief chapter on massage gives a description of the physiologic effects of massage and the principles involved in the various strokes commonly used. There are several valuable and interesting chapters on closely allied topics, such as occupational therapy, climatotherapy and spa therapy. The latter part of the book includes practical suggestions on applied physical therapy for diseases of all the systems of the body. The appendix contains a valuable discussion of the requirements for physical therapeutic apparatus as outlined by the Department of Hospitals of New York City, which can serve as a guide for physicians in general practice who wish to buy such equipment.

A Textbook of Histology: Functional Significance of Cells and Intercellular Substances. By E. V. Cowdry, Professor of Anatomy, The School of Medicine, Washington University, St. Louis. Third edition. Cloth. Price, $7. Pp. 426, with 317 illustrations. Philadelphia: Lea & Febiger, 1944.

In the new edition the author has adhered to the method of presentation outlined in the preface of the first edition. He rejects the usual manner of approach in which the material is treated in more or less isolated units of the order of cells, tissues and organs. Since the properties of cells and tissues are greatly dependent on the environment in which they exist, the author attempts "to build up, as the discussion advances, a conception of cells and elementary tissues in the many environments in which they normally exist." The author has abandoned the usual order of teaching histology and has arranged the material around the blood vascular system as the principal integrator. The result is an interesting book which deserves the close attention of those who have experienced difficulties in teaching histology as though it were built up of isolated units. It is debatable, however, whether the arrangement of the material in this book actually contributes to the removal of these difficulties. For example, the deferment of the discussion of the elementary tissues to practically the end of the book complicates unnecessarily any teaching program of histology. The author could probably have achieved his purpose of synthesis and integration by following a more logical, analytic order.

This edition is considerably simplified. Fortunately, this has not been accomplished at the expense of the newer experimental work, which is well represented. The original illustrations are good and those taken from the literature are chosen with care. This book will undoubtedly stimulate the student and arouse his interest in modern experimental histology.

Large Scale Rorschach Techniques: A Manual for the Group Rorschach and Multiple Choice Test. By M. R. Harrower-Erickson, Acad. Dip., Ph.D., Research Associate, Department of Neuropsychiatry, University of Wisconsin, Madison, and M. E. Steiner, B.A., M.A., Personnel Section, General Electric Company, Bridgeport, Conn. Cloth. Price, $8.50. Pp. 419, with illustrations. Springfield, Illinois: Charles C Thomas, 1945.

The present volume represents a well written, comprehensive manual of large scale Rorschach technics by writers who are well known and respected for their work in this field. Methods used for group testing and multiple choice tests, according to the Rorschach (ink blot) method are clearly delineated. The Rorschach test is rapidly coming to be regarded and better utilized as a method of estimating emotional stability and ego strength and as a prognostic indicator in various types of psychologic disturbances. The authors of this manual have shown how the technic can be administered to groups and in this way greatly extend the scope of the original method. They have also devised a new test which can be utilized for screening or eliminating poorly adjusted persons from the armed forces even though the persons giving the test have not had extensive training in the Rorschach technic. The manual contains also a section devoted to military psychiatry which demonstrates the utilization of the Rorschach test for differential diagnosis of psychiatric casualties. The book is well indexed for handy reference and contains a separate index for the authors referred to in the text. The work represents an extremely valuable contribution to both military and civilian psychologic investigation.

Textbook of Medical Treatment. By Various Authors. Edited by D. M. Dunlop, B.A., M.D., F.R.C.P., Professor of Therapeutics and Clinical Medicine, University of Edinburgh, L. S. P. Davidson, B.A., M.D., F.R.C.P., Professor of Medicine and Clinical Medicine, University of Edinburgh, and J. W. McNee, D.S.O., D.Sc., M.D., Physician, H. M. the King in Scotland. With a foreword by the late Professor A. J. Clark, B.A., M.D., D.P.H. Third edition. Cloth. Price, $8. Pp. 1,218, with 26 illustrations. Baltimore: William Wood & Company, 1944.

This book, although the third edition since 1939, has several deficiencies. For example, the index contains no reference to penicillin and none to staphylococci, although there are several references to streptococci. Under the heading mercurial diuretics the index has a cross reference to mersalyl, a single member of the group. The discussion of active immunization against tetanus with toxoid is exceedingly brief and mentions only that "active immunization against tetanus has recently been introduced in the British army. The course consists of two doses of 1 cc. of tetanus toxoid with an interval of six weeks between the injections." Thiouracil (incidentally with a misprint) is mentioned in two sentences. After the war it should be possible to revise this book more extensively, eliminating most of the defects which now exist.

Bacteriology for Medical Students and Practitioners. By A. D. Gardner, D.M., F.R.C.S., Professor in Bacteriology, University of Oxford, Oxford. Third edition. Cloth. Price, $2.50. Pp. 264, with 31 illustrations. New York & London: Oxford University Press, 1944.

This pocket size book presents shortly, readably and relevantly, without details of technic, information in bacteriology which the medical student or practitioner should know. The success of the book is evident from the fact that it is now in its third edition. The present volume has been brought up to date and the last chapter has been enlarged by the inclusion of new and partly unpublished matter on disinfection and chemotherapy. The volume may be recommended to medical students and practitioners, though it must be supplemented when detailed knowledge of a subject is desired.

Bibliographie der Luftfahrtmedizin. Zweite Folge: Eine Zusammenstellung von Arbeiten über Luftfahrtmedizin und Grenzgebiete 1937 bis Ende 1940. Von Dr. med. Ingeborg Schmidt. In: Luftfahrtmedizin, Band 8, Heft 1. Paper. Pp. 128. Berlin: Springer-Verlag, 1943.

This is a bibliography of aviation medicine divided according to subject and author. There is first a list of books and monographs followed by subjects alphabetically from aeroembolism to teeth. The subject headings are in German, but the titles or articles in English and other non-German languages have not been translated. The list of classified references occupies ninety-three pages, with approximately twenty-five references to the page.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

INTOXICATION AND MIXING ALCOHOLIC DRINKS

To the Editor:—**Is there a greater tendency toward drunkenness if alcoholic beverages are mixed successively, i. e. if whisky is followed by gin or scotch or by beer or wine? Some maintain that the mixing is not a factor in drunkenness but that intoxication is dependent on the amount of liquor consumed.**

M.D., Pennsylvania.

ANSWER.—The concentration of alcohol in the blood and brain is determined chiefly by the amount of alcohol consumed. However, the rate of absorption also affects the concentration reached, since if it is slow some of the alcohol may be destroyed or excreted before the peak is reached. Absorption may be delayed by dilution or by delay in emptying the stomach, since more rapid absorption occurs below the pylorus. The greater intoxicating effect of liquor taken on an empty stomach than that taken after a meal has been often remarked. Water or foodstuffs taken with liquor may be expected, accordingly, to lessen the intoxicating effect. Excitement or activity may also slow absorption of alcohol. Factors accelerating gastric emptying increase the effect of alcoholic beverages. Individual susceptibilities may depend on the previous experiences and associations of the drinkers.

Many experienced drinkers claim that mixing drinks accelerates their absorption and the rapidity of onset and depth of intoxication. It has also been reported that mixing drinks hastens the onset of nausea, vomiting and the unpleasant aftereffects following a drinking bout. It is possible that the olfactory and gustatory effect of mixed drinks may be to accelerate gastric emptying and hence absorption. Also the addition of water to single drinks may result in diluting the alcohol to a greater extent than the dilution produced by mixing several beverages each of which contains considerable alcohol. The mixed drink may not only represent a higher alcohol content than the single beverage, then, but the drinker, ignoring this fact, may consequently drink more when he mixes his drinks, without realizing the fact. Despite the general belief in the greater potency of mixed drinks, it is probable that the differences are really quite small and that an equal amount of alcohol, taken in the same total volume of liquid, would produce practically equivalent effects.

CHRONIC URTICARIA IN WARM WEATHER

To the Editor:—**A patient has chronic urticaria which came on two days after vaccination, at the age of 6; it occurs only in hot weather. The history and physical examination give no clues as to any cause except the vaccination. Would you, if possible, suggest treatment, bearing in mind the fact that all orthodox treatment has already been given?**

M.D., Massachusetts.

ANSWER.—It is well to have the parenthetical "if possible" included in this question. The treatment of chronic urticaria of unknown cause is one of the most difficult problems in medicine. It is a problem that only future research on the nature of urticaria can solve satisfactorily. However, with the hope that some constructive suggestion may be made in this case, the following remarks are primarily directed at the etiologic possibilities suggested by the brief history given. First, it is improbable that a vaccination done at the age of 6 (presumably years ago, since the term "chronic urticaria" and "occurs only in hot weather" are used) should continue to be a causative factor of the condition. The recurrence during hot weather suggests a variety of possible causes: (1) heat or sensitivity to sunlight; (2) allergy to pollen or insect bites (mosquitoes?); (3) drugs used primarily in summer, either internally or externally; (4) dermatophytoses with an urticarial "id" reaction (unusual, but 1 such case has been seen by the writer); (5) allergy to foods ingested only in the summer.

These are a few suggestions that occur because of the limitation of the condition to the summer months. The investigation of these and other possibilities requires a carefully planned campaign for each possible etiologic factor. Without a continued, untiring etiologic search, most efforts are of little help.

As for therapy while the search for cause goes on, two more recent suggestions in the literature (since the usual measures have already been tried) are worth suggesting: first, the use of nicotinic acid and calcium lactate (Chambers, D. C., and Bernton, H. S.: *J. Allergy* **15**:141 [March] 1944) and, second, the injection of histamine-azoprotein (hapamine). The most recent article on the latter therapy is by M. B. Cohen and H. J. Friedman (*J. Allergy* **15**:245 [July] 1944. These authors give a bibliography on the use of this histamine-protein conjugate.

SPONTANEOUS PNEUMOTHORAX IN CHILD

To the Editor:—**A girl aged 7, with a normal history except for influenza six months ago, recently had shortness of breath and a rapid heart action. A complete pneumothorax of the left lung was revealed by x-ray examination and fluoroscopy. This appeared to be still open at the first examination: the ribs were much more widely separated on the left side, with the heart and the mediastinum displaced to the right. After weekly observation under the fluoroscope for three weeks the lung gradually began to expand and in three weeks was completely expanded with the exception of a small amount of fluid, which soon disappeared. X-ray examination after expansion showed a normal left lung. The child gave a negative reaction for tuberculosis with the Pirquet test. I have been treating diseases of the chest for many years, and this is the first case I have seen of pneumothorax in a young child without any apparent cause. Is this condition rare, or have I been missing something?**

E. E. Clovis, M.D., Wheeling, W. Va.

ANSWER.—Spontaneous pneumothorax occurs much less frequently in children than in adults both young and old. The most common cause in all patients is rupture of a thin walled bleb, a bulla or a pulmonary cyst, either congenital or acquired, at the surface of the lung. Blebs and even acquired cysts may be localized exaggerations of the lesions of a generalized pulmonary emphysema or of a lobar or total unilateral obstructive emphysema due to a check valve mechanism produced by localized swelling of the bronchial mucosa (which may have been produced by the influenza in this patient). They may be the results also of an intrabronchial foreign body or neoplasm or of extrabronchial pressure.

Because of the thinness of their walls, some blebs and acquired cysts cannot be seen in roentgenograms made either before the occurrence of a spontaneous pneumothorax or after expansion of the collapsed lung. There is a strong tendency for spontaneous pneumothorax to recur in the course of months or years, and occasionally the condition occurs in both sides of the chest.

SURGERY OF THYROGLOSSAL DUCT

To the Editor:—**Frequently in descriptions of the technic employed for the dissection of a thyroglossal cyst, mention is made of section of the hyoid bone. No report has been found as to how much dysfunction may occur following such a procedure, and comment on this possibility would be appreciated. Is any attempt made to suture the bone into approximation?**

M.D., Illinois.

ANSWER.—Any operative procedure on a thyroglossal duct cyst or sinus which fails to remove the entire tract results in failure, that is, recurrence or persistence of the draining sinus. Since the tract passes immediately below, above or more commonly through the hyoid bone and through the middle of the tongue, and since it is not always possible at operation, because of its small size and friability, actually to trace the tract throughout its entire course, experience has proved that the radical operation of Sistrunk is necessary for cure in a large percentage of cases. This operation consists in removing a cylinder of tissue immediately surrounding the normal pathway of the tract and including the central segment of the hyoid bone, The ends of the hyoid bone are approximated with stitches through the periosteum. Whether the union is a bony or fibrous one is not known; however, after operation there is no detectable evidence of disability from this source.

AMINO ACIDS IN PYLOROSPASM

To the Editor:—**Please evaluate the use of the amino acids in pyloric obstruction other than to supplant the loss of proteins. Do the amino acids relieve pyloric stenosis in the newborn? My practice is to operate in cases of pyloric stenosis as soon as they are diagnosed rather than to wait until alkalosis, acidosis or dehydration is evidenced. Will the amino acids relieve pylorospasm?**

G. J. Searle, M.D., Mansfield, Ohio.

ANSWER.—Administration of amino acids has not been demonstrated to have a specific effect on hypertrophic pyloric stenosis or on pylorospasm in the infant, so far as can be determined. However, amino acid-saline infusions have proved to be useful as a supplement to glucose solution in cases of pyloric obstruction in which parenteral feeding and fluid administration are required. In neglected cases showing pronounced dehydration and inanition from continuous vomiting, such replacement therapy is indicated as an essential feature of preoperative and postoperative management.